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of the
INDIAN MEDICAL ASSOCIATION

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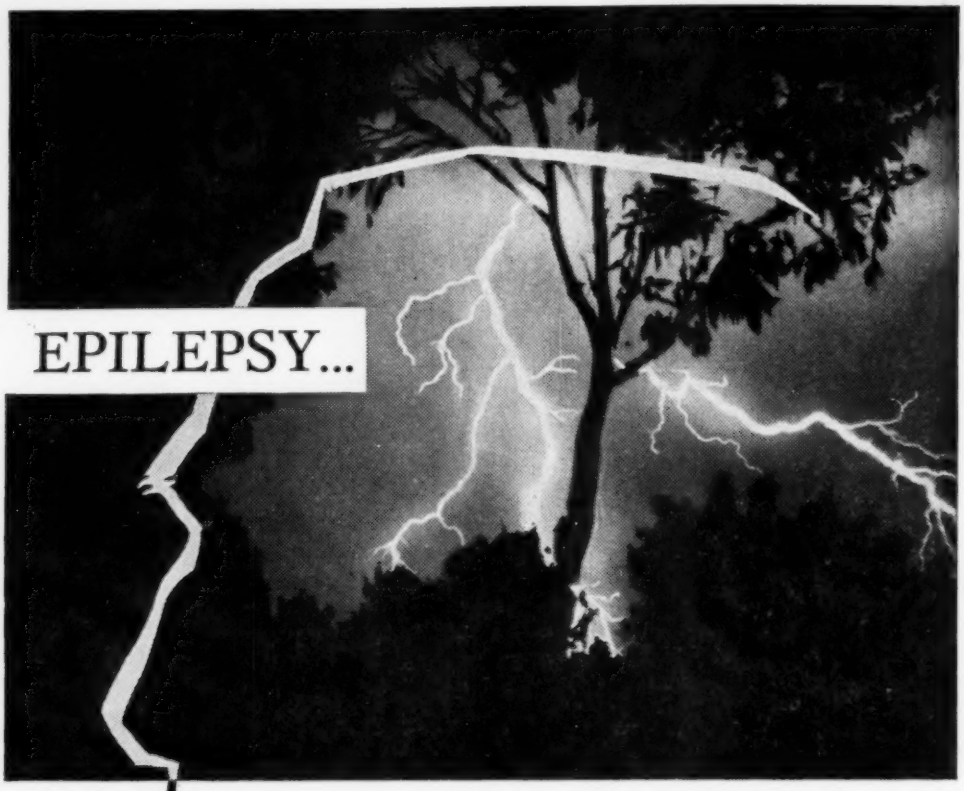

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TABLE OF CONTENTS

ORIGINAL ARTICLES :	Page
1. Tropical Eosinophilia—R. N. Chaudhuri ...	195
2. Scrub Typhus Treated with Antibiotics —T. N. Mathur, K. N. Datta and R. N. Sood	201
3. A Preliminary Study on the Treatment of Malaria with Quinine-Calcium Gluconogalacto-gluconate—M. N. Jindal	204
4. Complement Values in Experimentally Induced Deficiency States in Guinea Pigs—C. Mohan Rangam, J. Chandra and A. N. Rai Chowdhary	205
CASE NOTES :	
1. Neuromyelitis Optica with Xanthochromia of Cerebrospinal Fluid—H. Ganguli and I. S. Roy	208

CASE NOTES—*Contd.*	Page
2. The Problem of Acute Pyogenic Infection in Patients Hypersensitive to Penicillin —P. Mazumder	209
EDITORIAL :	
Tropical Eosinophilia and Parasitism	210
CURRENT MEDICAL LITERATURE	213
CURRENT TOPIC	216
NOTES AND NEWS	226
CORRESPONDENCE	229
REVIEWS	230

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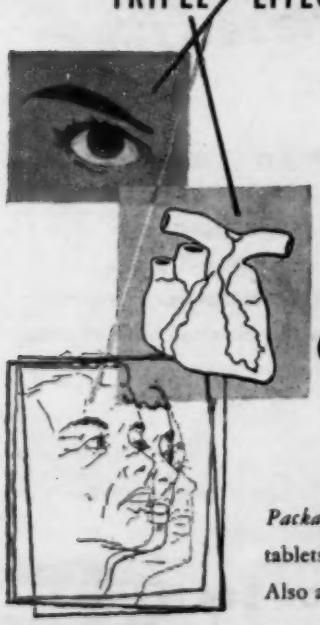

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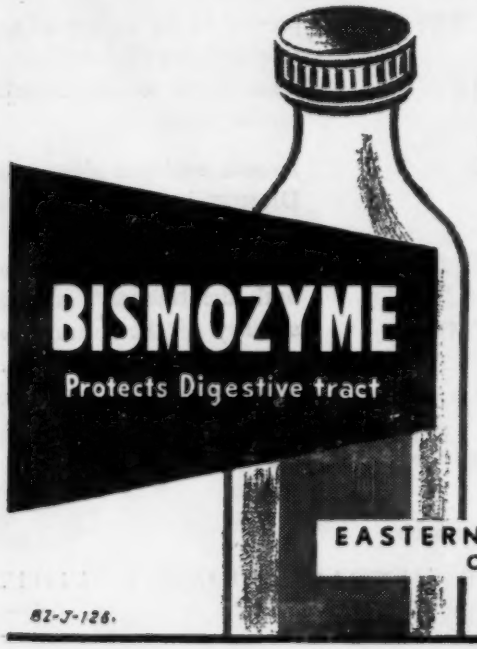

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INDEX TO ADVERTISERS

	Page
Adcee Ltd.	x
Allied Photographics Private td.	xix
Alembic Chemical Works Co. Ltd.	xxv
Allen & Hanburys Ltd.	vii
Amalgamated Chemicals & Dyestuffs Co., Private Ltd.	xxi
Bengal Chemical & Pharm. Works Ltd.	Front Cover
British Felsol Co. Ltd	xxvi
British Drug Houses (I) Private Ltd.	xxvii
Burroughs Wellcome & Co. (I) Private Ltd.	xiii
Capco Private Ltd.	xxix
Ciba Pharma Private Ltd.	xi
Cipla Ltd.	xxiv
Corn Products Co. (India) Ltd.	xiv
Cow & Gate Ltd.	xxi
Crookes Laboratories Ltd.	xvii
Dumex Private Ltd.	xxii
Eastern Drug Co. Ltd.	ii
East India Pharmaceutical Works Ltd.	xx
Emsons Pharmaceutical Works	xxviii
Frank W. Horner Ltd.	xxiii
Geoffrey Manners & Co. Private Ltd.	xviii
Gluconate Ltd.	xxviii
Government of West Bengal	iv
Horlicks Ltd.	xv
Imperial Chemical Industries (I) Private Ltd.	2nd Cover
Indian Oxygen & Acetylene Co. Private Ltd.	vi
James A. Jobling & Co. Ltd.	viii
John Wyeth & Brother Ltd.	xxx
Kesari Kuteeram Private Ltd.	viii
Kishore Nursing Home	xxviii
Lederle Laboratories (I) Private Ltd.	i
Nestle's Products (India) Ltd.	xvi
Oriental Pharmaceutical Industries Ltd.	xxviii
Parry & Co. Ltd.	xii
Pannalal Brothers	xxvii
Pfizer Eastern Corporation (Ravison Pharm. Private Ltd.)	Back Cover
Raptakos, Brett & Co. Ltd.	xv
R. G. Kar Medical College Ex-Students Association	Front Cover
Standard-Vacuum Oil Co.	ix
Standard Pharmaceutical Works Ltd.	xii
Sanitex Chemical Industries Ltd.	x
Smith Stanistreet & Co. Ltd.	xxvi
Unichem Laboratories	xxiii
Voltas Ltd.	v
W. T. Suren & Co. Private Ltd.	xiv

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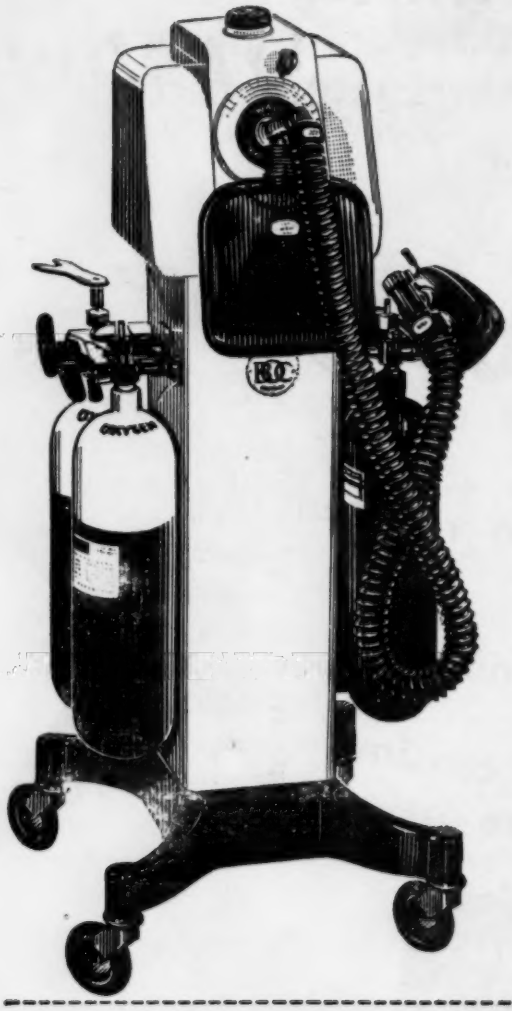

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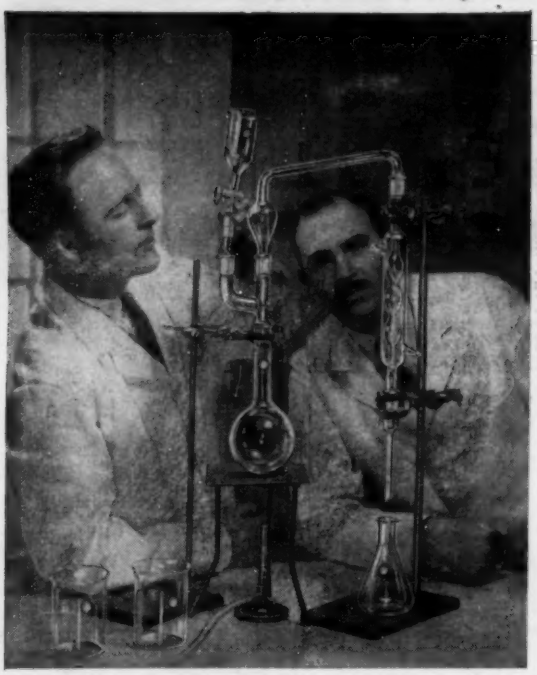

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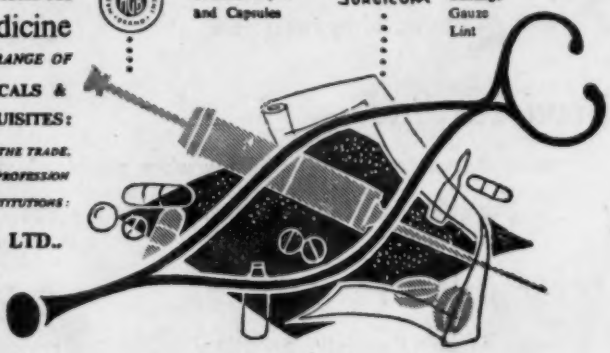

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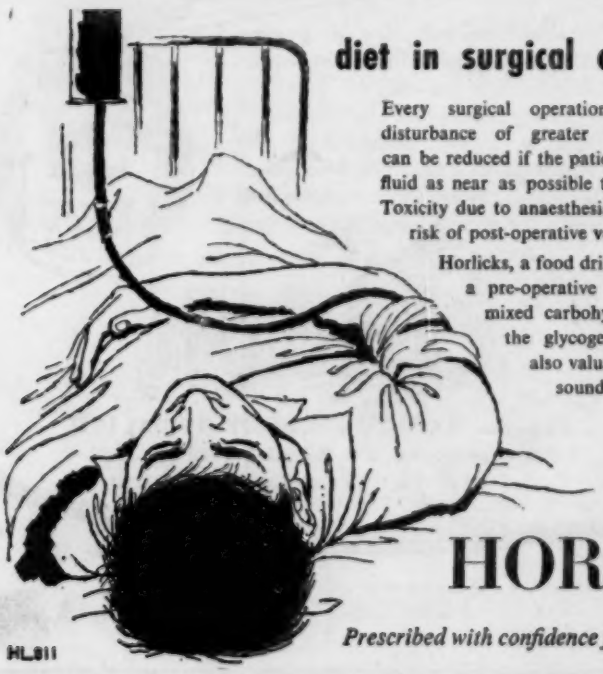

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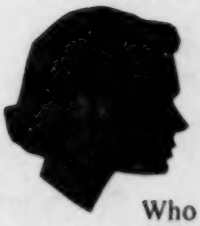

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ORIGINAL ARTICLES

TROPICAL EOSINOPHILIA †

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Introduction

Tropical eosinophilia is an established clinical entity, quite common in this country. It is characterised by four salient features, viz., persistent or recurrent cough with or without asthma, eosinophilia high enough to produce leucocytosis, radiological changes in the lung field in about half the cases and apparently specific effect of arsenic.

Weingarten (1943) described a large series of cases in India with cough and dyspnoea somewhat resembling asthmatic attacks, massive eosinophilia, radiological picture of mottling of the lungs, and response to arsenical treatment. At first it was thought to be a new syndrome which had hitherto passed unnoticed by other clinicians. But three years before Weingarten's paper appeared, Frimodt-Möller and Barton (1940) had described a larger group of 175 patients seen during 15 years in the Madanapalle Sanatorium, South India, where they had been admitted on suspicion of tuberculosis. The clinical picture was closely similar, and after prolonged observation the authors came to the conclusion that it was a benign condition of allergic origin.

Weingarten did not seem to be aware of this important paper by Frimodt-Möller and Barton. Weingarten's observation was based on a study of 81 cases coming from all ranks, age and sex. There was no evidence of familial, occupational or seasonal susceptibility. He was of the opinion that the condition was not an allergic state and he stressed the influence of environment as an aetiological factor. Chaudhuri (Editorial, 1943) suggested that the paroxysms of cough, eosinophilia and pulmonary infiltrations were the result of allergic response to some antigen. Chakravarty and Roy (1943) reported one case which had urticaria in addition to other symptoms.

Though the chief focus of the disease as described by the above authors appears to be in India, it was not unknown in other countries. For instance, Loeffler (1932, 1936) in Switzerland noted a syndrome in which eosinophilia and cough were associated with pulmonary infiltration which was transitory. Bass (1931) in the U.S.A. reported on high eosinophilia with bronchitis, asthma and pulmonary infiltrations, while de Langen and Djamil (1923) in Dutch East Indies published some observations on idiopathic 'hypereosinophilia'.

But for the record of still earlier observations of similar nature we must go further back and that too in this country itself. Not long ago the writer had a pleasant surprise in coming across a paper in the *Calcutta Medical Journal* by Roy and Bose (1918) based on a study of as many as 140 cases of asthma, the majority of whom had leucocytosis (the highest being 58,000 per c.mm.), the average proportion of eosinophils being 48 per cent and the maximum 89 per cent. The authors noted the intimate relationship between asthma and eosinophilia and treated these patients with subcutaneous or intramuscular injections of soamin and alkalies by mouth to keep the urine alkaline. 75 to 80 per cent of the cases were fully cured and remained free from attacks. About this time Ghosh (1918) noted an important fact that cases

† Based on a lecture delivered at the Indian Medical Association, Calcutta Branch, in April, 1950.

'in which there is no eosinophilia do not improve well' with soamin.

It thus appears that Roy and Bose's paper is perhaps the earliest record of "tropical eosinophilia", at least in this country, and if credit is due to anybody it should be given to these authors. The great merit of Weingarten's paper lies in the fact that he put the treatment on a more rational basis. One of his patients had contracted syphilis, for which he gave neoarsphenamine injections and was struck with their dramatic effect on the blood and x-ray picture. Subsequently he obtained uniformly good results with this form of treatment. Soon after Weingarten's publication Chaudhuri (1943) reported a typical case entitled eosinophil lung.

Pathology

Because of the relatively benign course of the disease post-mortem observations have been very limited. Von Meyenburg (1942) on autopsy study of 4 soldiers suffering from Loeffler's syndrome, who died accidentally, described that the lesions were like lobular pneumonia (diffuse bronchopneumonic patches) with exudation in the alveoli containing 70 to 100 per cent eosinophil cells and also eosinophilic infiltrations of the alveoli and interstitial tissue. Giant cells formations were also observed. Broch (1953) reported in another autopsy that around some branches of bronchi there was intense leucocytic infiltration with a remarkably high proportion of eosinophil cells. Harkavy (1943) attributed the fugitive pulmonary infiltrations to congestion, oedema and thrombi in small blood vessels as well as infiltrations of the interalveolar septum with eosinophils and other cells. He also observed evidence of arteritis. Bayley *et al*, (1945) reported about the post-mortem examination of a female who had asthma, bizzare x-ray changes and eosinophilia. Necropsy showed many irregular regions of increased density throughout the lungs. The histological appearance was that of an unusual type of organised pneumonia in which there were many eosinophils. In addition, thickening of arterial walls was noticed. Besides, bronchial lesions were also observed like those occurring in bronchial asthma *viz.*, hypertrophy of the muscle of the bronchial wall though not so marked, plus eosinophilic exudate infiltrating the bronchial wall leading to the use of the term 'eosinophilic bronchitis or bronchiolitis' by Meyenburg as occurring in Loeffler's syndrome. Granulomatous lesions have also been described. In India, Viswanathan (1947) described scattered areas of interstitial fibroblastic proliferation and eosinophilic infiltration with some of the adjacent alveoli containing macrophages. A few areas containing giant cells (non-tuberculous) were also noted. According to him the changes were suggestive of chronicity. He further observed that inoculation of guineapigs with brain and lung filtrates yielded no positive result.

Clinical Features

Features of interest observed in 167 cases admitted to the hospital under the writer's care are briefly presented in this paper.

One of the characteristics was the intermittent character of the attacks appearing as bronchitis, or cold and cough ; sometimes the patients were entirely symptom-free. Some had bouts of fever while many were afebrile. Ten patients complained of indefinite but troublesome pain in the chest. Three had spitting of blood.

The liver was enlarged in 52 cases, the spleen in 14 and the lymph nodes in 5.

Lung symptoms were not constant and very often without asthma. Certain atypical cases were encountered. As many as 42 patients had no pulmonary complaints, and were admitted for some other ailments, mostly gastro-intestinal and the condition was detected accidentally. About 40 per cent of cases had evidence of upper respiratory tract infection or allergy. Tonsillectomy was done in 2 boys with practically no effect on the eosinophilia. In another case with imperfect response to arsenical injections tonsillectomy was of value.

Influence of associated infection—Eosinopenic response to acute febrile attacks due to associated infections was observed in 8 cases (Sen *et al*, 1956). It was noted that there was a remarkable fall in circulating eosinophils, though temporary, during the fever, but in most of them the count slowly began to rise within a week after the fever subsided and even reached near about the former level.

The infection in all cases was either of the upper respiratory tract or similar to one causing 'short fever' except in one who had measles. It is probable that in acute infections there is hyperfunction of adrenals with liberation of epinephrin-like substance causing temporary depression of blood eosinophils through the pituitary-adrenocortical axis.

Laboratory Findings

Blood-eosinophils—The most important feature of the cases was high eosinophilic leucocytosis, the absolute number of eosinophils in this series being 2,000 to 40,050 per c.mm. and the total white cell count varying from 10,000 to 45,000 per c.mm. In the differential count the eosinophils ranged

from 20 to 90 per cent of the total white cells. The eosinophils were essentially mature segmented forms, not differentiated from normal cells. Occasionally some polylobular or vacuolated cells were found. No blast cells were seen. The counts fluctuated without any apparent cause. There was no constant correlation between the degree of eosinophilia and the intensity of symptoms.

Bone-marrow—Bone-marrow smears showed increase of eosinophilic cells at all stages of development with relative depression of neutrophilic cells. Normoblasts in general constituted 20 to 25 per cent of nucleated cells. Megakaryocytes appeared active.

Blood culture—The blood of a small number of patients was cultured during the febrile period. From the blood of three persons a fungus of the genus streptomyces was isolated, but on animal inoculation it proved to be non-pathogenic (Neogy *et al*, 1954) and was regarded as a contaminant.

Wassermann and Kahn tests—False-positive but Kahn-negative reactions were obtained in a proportion of cases.

Liver biopsy—The liver tissue obtained by needle biopsy from five patients showed cellular, mostly eosinophilic infiltration along the portal tracts in addition to large number of eosinophils in the sinusoids.

Helminthic infection—About 25 per cent of cases had helminthic infection including ascaris ova in the faces of several patients and microfilaria in the peripheral blood of two.

Mites—A search for mites in a series of cases following the technique of Carter *et al* (1944) was made usually with negative results (Chaudhuri *et al*, 1953).

Spirochaetes—A search for spirochaetes was made in samples of bowel mucus obtained by washing out the lower bowel with a pint of distilled water after an enema, and also in sputum. Out of 18 cases 16 showed spirochaetes in the bowel mucus and 8 in the sputum in variable numbers. For a comparison, 13 cases with other ailments were examined, two of them showing spirochaetes in the sputum and 2 in the bowel mucus. There appeared to be three types of spirochaetes that were found in small or large numbers viz., short 'S'-shaped forms, longer and coarser ones and very fine close coiled spirochaetes.

X-ray findings—Radiologically mottling, increased hilar shadows and increased striations were frequent findings in the lung field often occurring in combination. 'Snow-storm' appearance, mottling—fine or coarse, generalised or localised, and ground-glass appearance were the terms used by the radiologist in typical cases. Bronchial markings were often visualised even in the periphery of the lung field and basal emphysema was sometimes noticed. The extent of the radiological findings did not always appear to be correlated to the severity of the symptoms. The eosinophil count often waxed and waned but not the mottlings, except in a few cases, though the patient might be free from symptoms. The radiological abnormalities in the lungs often regressed after treatment, and often reappeared with relapse. In others these changes persisted in spite of clinical cure. The pulmonary lesions were not necessarily dependent on the duration of the disease. Evidence of associated bronchiectasis, atelactasis and active or arrested tuberculous lesions was noticed in a few patients.

Treatment

Arsenic—Most of our earlier cases had intravenous arsenical injections viz., neoarsphenamine or oxophenarsinehydrochloride in doses of 0·3 g. to 0·45 g. and 0·02 g. to 0·04 g. respectively given at interval of about 5 days, the average total number of injections being 6. Later, intramuscular injections of diethylamine acetarsol in a dose of 3 c.c. for the adults, each c.c. containing 0·05 g. of pentavalent arsenic, at intervals of 3 days were used. The vast majority of the cases responded well to 6 to 10 injections. Many patients exhibited an initial reaction with a rise in eosinophils and sometimes exacerbations of symptoms followed by subsequent improvement. In many, the response was striking, in some it was rather slow, the eosinophil count not returning to normal level until weeks after the completion of treatment, while a few appeared refractory. For instance, one child was admitted for generalised oedema diagnosed as 'nutritional oedema' which subsided with skimmed milk diet. Thereafter, the child had a migratory type of oedema (suggestive of Gnathostome infection) from time to time, sometimes with fever. This might not be a true case of tropical eosinophilia. No parasitic infection was demonstrated but the child had a high eosinophilic leucocytosis. A course of diethylamine acetersol was given without any effect whatsoever. In patients with chronic asthma and emphysema, the clinical improvement was not striking although the eosinophil level had come down with treatment. One or more relapses occurred in about 20 per cent cases after varying periods following apparent cure. One patient had as many as four relapses in six years. Untoward reactions were encountered by way of febrile attacks in a number of cases after each injection, agranulocytosis (Chaudhuri and Rai Chaudhuri, 1945) in one case and dermatitis in

two. Soamin was used in 10 cases, the initial dose for an adult being 2 gr. I.M. and subsequently in doses of 2 to 3 gr. at intervals of 2 days, on an average 25 gr. being the total dose used in 3½ weeks. All but one responded well and no untoward reactions were noticed. Oral preparations such as carbarsone were tried in a series of cases in doses of 1 tablet (0·25 g.) twice daily for 10 days folowed by a second course after an interval of 10 days. Acetarsol was also used in a number of patients. The response appeared to be slow; in some patients it was changed to arsenical injections. Fowler's solution was found ineffective.

Aureomycin—Aureomycin, (Chaudhuri, 1953) in doses of 0·25 to 0·5 g. 6 hourly for 10 days, was tried in 16 cases. Eight of them were cured (one of them required a second course); six had partial relief and 2 failed to respond even after the second course. The effect was striking in a few patients who were intolerent to arsenical injection.

Emetine—Emetine hydrochloride in doses of 1 gr. I.M. given on alternate days till a total of 6-10 injections caused a remarkable effect in 3 cases with *E. histolytica* in stools but failed in several others.

Diethyl carbamazine in daily doses of 12 to 16 tablets (50 mg. each) for 7-10 days was found fairly effective in 10 out of 12 patients, the eosinophil count in 4 of these cases being shown in the Table. It has been reported that the clinical results with piperazine derivative in doses of 13 mg. per Kg. for 4 days compared well with those obtained with carbarsone (Ganatra and Lewis, 1955). The effects of piperazine compounds on eosinophilia have also been observed by other workers (Martinez Baez and Tello de La Pena, 1952; Galliard and Lariviere, 1953; Friess *et al*, 1953; Faure *et al*, 1954).

Adrenalin—Adrenalin injections (Chaudhuri, 1951) ½ c.c. I.M. twice daily for 10 days caused temporary reduction of eosinophils in some cases but failed in others.

Other drugs—Antimony, bismuth, penicillin, streptomycin, sulpha drugs, antihistamins tried in a few cases appeared ineffective on eosinophilia.

Prednisone—The drug has recently been tried by us in 9 cases of tropical eosinophilia with quick effect, clinical, radiological and haematological in all but two. The dosage used was 10 mg. thrice daily for 7-10 days. One patient with severe asthmatic dysponea was relieved in a very short time. The circulating eosinophils were reduced to nearly normal limits within a week in most of them. The eosinophil count however tended to rise sooner or later after the completion of treatment, often associated with recurrence of symptoms and reappearance of radiological mottling in the lung field. According to Esselier *et al*, (1954) the decrease in circulating eosinophils after 'glucocorticoids' depends on inhibition of the release of eosinophils from the bonemarrow and on an increased destruction of eosinophils by the reticulo-endothelial system.

Aetiopathogenesis—A Discussion

In this condition there is increased production in the bone marrow of eosinophil cells which circulate in the blood and also infiltrate the tissues, especially the lung. The skiagrams of the pulmonary lesions have been interpreted as due to oedema, exudate, eosinophilic infiltration, atelectasis or pneumonitis. The reaction may be of short or of long duration; it may involve alveoli and also bronchi; asthma perhaps occurs when the latter is affected. We know how to diagnose and how to treat the disease but without a knowledge of the causative agent or how it is disseminated. The fact that the disease responds to treatment with a variety of unrelated medicaments further complicates the search for the cause of the condition.

The two important possibilities are that it is an allergic condition and that it is an infection. It may be a combination of both, i.e., an allergic

Table—Showing the Effect of Piperazine Compounds on Eosinophilic Count in 4 Cases

Patient, age (in years) & sex	Initial count Total per c.mm.	%	Count per c.mm. after completion of course in weeks									
			1st		2nd		3rd		4th		5th	
			Total	%	Total	%	Total	%	Total	%	Total	%
S.B. 19, F. ...	24,864	74	17,520	73	28,470	78	21,760	68	—		4,050	25
A.C. 36, M. ...	7,040	40	4,556	34	2,448	24	4,416	32	1,880	20	1,320	15
J.S. 20, M. ...	13,440	60	8,400	50	—		5,280	40	3,060	30	1,760	20
B.D.C. 23, M. ...	5,712	32	1,360	16	864	12	—		—		—	

reaction to some underlying infection or infestation. But so far no single antigenic substance or infective agent has been detected. Helminths, mites, bacteria, spirochaetes, and virus have been suspected. This would indicate that there is possibility of multiple infecting agents of the disease and that the pulmonary changes may be due to hypersensitive reaction of the lung tissue to one or more varieties of allergens. Respiratory symptoms, eosinophilia, lung infiltration, variable effect of adrenalin and dramatic response to A.C.T.H. (Sanjivi *et al*, 1955), cortisone and hydrocortisone (*vide supra*) though temporary are indirectly suggestive of an allergic process which is linked with eosinophilia. Most of the conditions with prominent eosinophilia are considered to have an allergic basis. The commonest mechanism of eosinophil increase in blood and tissues is believed to result from an antigen-antibody reaction, i.e., a response of sensitised tissue to contact with sensitising antigen, as for examples, in serum sickness, parasitic infections, etc. It should be noted that sensitisation itself does not evoke eosinophilia, unless the sensitive person has been re-exposed to the antigen. Moreover, antigen-antibody union may occur during re-exposure without any increase in circulating eosinophils; consequently eosinophilia is not an invariable finding in allergic cases (Editorial, 1953).

The apparently specific effect of arsenic, aureomycin and piperazine compound in the majority of cases points to infection of some kind. If it is due to infection, blood borne infection with bacteria or virus seems rather unlikely since transfusion of 250 c.mm. blood from patients with marked eosinophilia and lung symptoms caused no significant reaction in any of the three recipients at least within the period of several months so far observed by us. The therapeutic efficacy of the drugs mentioned, particularly arsenic and piperazine, is suggestive of infection with intestinal or tissue parasites while the circulatory and respiratory changes may be an allergic response to it. Microfilaria have been reported to be present by some workers (Van der Sar and Hartz, 1945) in the gland biopsy of massive eosinophilic cases, while others have failed to confirm this finding. In some areas of Africa, infestation by *Filarial worm Acanthocheilonema perstans* is known to cause eosinophilia of 70 per cent or more (Editorial, 1948). Loeffler's syndrome was attributed to migration of ascaris larvae in the lung and also to allergic reaction. According to Westwood and Levin (1951) ascariasis was a common association with the condition. In Frimodt-Möller and Barton's series, 48 per cent had infection with intestinal parasites, but the infection rate was even less in those with the highest eosinophil count. Ball (1950) also found intestinal parasites in 48 per cent of his cases against 58 per cent among a large series of control. In our series ascaris ova were found in the stool of several cases and microfilaria in the blood of two patients only. But the proportion of cases showing ascaris or other helminthic infection was not higher than that in our hospital cases suffering from other diseases. Treatment of intestinal helminths has not significantly influenced the eosinophilic condition. But failure to demonstrate parasites or ova cannot definitely invalidate the parasitic role in this condition. There is another clinical entity of comparatively recent recognition, known as visceral larva migrans, believed to be due to the invasion of human system by nematode larvae of species naturally adapted to hosts other than man (Beaver *et al*, 1952, Smith and Beaver, 1953). The clinical event is characterised by symptoms of chronic hypereosinophilia, hepatomegaly, moderate pulmonary infiltration, fever, cough, and hyperglobulinaemia.

It is worthwhile to mention in this connection that the author (Chaudhuri and Chakravarti, 1949) has noted an increase in the globulin content of blood in a number of patients suffering from tropical eosinophilia. The eosinophilic invasion of hepatic tissue revealed by liver biopsy, stated before, is also a common occurrence in visceral larva migrans.

Spirochaetal infection is a probability in view of the ready response to arsenic and frequent Herxheimer type of reaction in the early phase of treatment. Spirochaetes have been found in the sputum by Shircore (1951) in Africa and in the faeces by Ganatra and Lewis (1955a) in Bombay. We have also found spirochaetes in samples of bowel mucus and sputum from such patients more often than in control or treated cases. But the fact that non-pathogenic spirochaetes are normally found in many mucous surfaces renders a search for the pathogenic one in such situations rather difficult.

Allergy in tropical eosinophilia would, therefore, appear to be of the infection-allergy type. In this condition there is an abnormal eosinophilic response or hyper-eosinophilia with lung invasion, the eosinophil cells having special affinity for tissue infiltration. Eosinophilic invasion of tissues is found in many pathological conditions, mostly allergic, with or without blood eosinophilia as manifested in the sputum of asthmatics, nasal secretions of vasomotor rhinitis, pleural fluid associated with tuberculosis or tropical eosinophilia, cerebro-spinal fluid in cysticercosis of the brain. Pyloric hypertrophy due to massive eosino-

philic infiltration has been observed in a patient with persistent eosinophilic leucocytosis. Recently we encountered a female patient with allergic dermatitis, the vesicle fluid containing numerous eosinophils but there was no blood eosinophilia. It is worth noting that the syndrome of tropical eosinophilia may be manifested in ways other than through the lungs. Abdominal symptoms have been noted with or without pulmonary symptoms in tropical eosinophilia (Chaudhuri *et al*, 1954). Forty two cases of the present series had mostly abdominal complaints and no respiratory symptom or sign. The antigen-antibody reaction appears to be of protean nature and may affect more than one organ. Eosinophilia also occurs in other conditions. In Hodgkin's disease there is more constant tissue eosinophilia than blood eosinophilia. Rise of eosinophil level in the peripheral blood has been noted after splenectomy (Chaudhuri *et al*, 1955 ; Saha and Chaudhuri, 1956) and following the administration of liver (Whitby and Britton, 1953). Very little is known of the actual mechanism that regulates eosinophil production.

The role of suprarenal cortex in the regulation of eosinophil level in the circulating blood is well recognised, but the precise modus operandi is yet to be known. It may be a depressive influence on the production centre at the marrow level, an increased destruction in the peripheral blood or a selective diversion to the accessible sinusoidal member of the reticulo-endothelial system like the spleen. This has also been conceived to be brought about as a result of an interference with the antigen-antibody reaction believed to be responsible for eosinophilia, either by inhibiting the antibody formation or influencing the reaction through an unknown mechanism. Adrenocortical functional integrity can be assessed with the help of Thorn's test, when 25 mg. of ACTH injected I.M. brings about a drop in the circulating eosinophils by about 75 per cent after a time interval of 4 hours and there is a corresponding rise of neutral 17-ketosteroid excretion in the urine. Adrenocortical activity in tropical eosinophilia militates against the suggestion of an acute infection, where it is usually a state of eosinopenia that is usually met with. Eosinophilia again is known to be a commonly encountered feature in allergic disease, ascribed to be an expression of antigen-antibody reaction, and an interference with the reaction may account for the favourable response of the condition to steroid hormones. This perhaps goes to lend a ready support to the allergic basis of tropical eosinophilia, where a measurable degree of eosinopenic response along with clinical and radiological improvement, though temporary, is obtained with ACTH and/or cortisone. Therapeutic effect of adrenocortical hormones in tropical eosinophilia resulting probably from a control of the allergic front is only short lived. Indeed, if the diseases were of the infection-allergy type, treatment of infection would obviously be essential. Recurrences or relapses that are not uncommon may be explained by subsequent allergic response precipitated by the same or allied allergen.

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SCRUB TYPHUS TREATED WITH ANTIBIOTICS

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It has been seen that cases of fever get admitted to the hospitals in Karnal District in greater number during and after the rainy season. Some of these cases on admission are toxaemic, stuporose, drowsy, delirious, mentally dull, apathetic and prostrated. Some of them are even unconscious and have rigidity of the neck and may be generally mistaken for cases of meningitis. Some cases of this type came to our notice when scrub typhus from Punjab was reported (Mathur and Suri, 1953 ; Mathur and Datta, 1954). Chaudhuri and Chakravarti (1949) reported 20 cases of scrub typhus, only three of whom, showed signs of meningeal irritation and nuchal rigidity. Five cases of scrub typhus (Table 1) mistaken for cases of meningitis are described.

Case 1—C.D., a 55 year old man, was admitted on 7-9-55 with a history of 11 days' continuous fever, becoming unconscious and delirious a week after the onset of the fever. He was incontinent of urine. There was no rash or eschar, the neck was rigid. He was put on sulphadiazine and penicillin but as there was no improvement even after 3 days, a lumbar puncture was done. The fluid was under normal tension and clear. Blood culture was sterile. Widal showed a titre of 1 in 50 for T.O. only. The Weil-Felix test, however, showed a titre of 1 in 500 for OXK, OX2 and OX19 being negative. A diagnosis of scrub typhus was made and the patient was put on chloramphenicol 250 mg. six hourly. The response was immediate and after 1 g., the drug was discontinued and he was put on sulphadiazine and penicillin with the result that two days later his fever relapsed. He was again put on the same dose of chloramphenicol. His fever came down (Fig. 1), his mental condition cleared up and he was

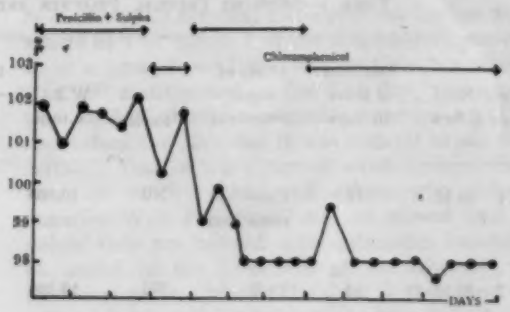

FIG. 1—SHOWING RESPONSE TO ANTIBIOTICS (CASE 1).

discharged cured from the hospital on 26-9-55. His blood was again tested on 13-9-55, i.e., three days after the first test, it showed a rise in titre of OXK from 1 in 500 to 1 in 1225.

Case 2—D.S., a thirty five year old farmer, was admitted on 19-9-55 with history of fever for 14 days. On examination the patient looked seriously ill and had a vacant expression responding only when called loudly. He was incontinent of urine. The neck was slightly rigid. Plantar reflexes were normal. Because of the slightly raised total leucocyte count and the increase of polymorphs (Table 1) and stiffness of the neck, he

was put on 4 lakh units of procaine penicillin on 19-9-55. This was repeated on 20-9-55 but his condition became more serious. Scrub typhus was suspected on 21-9-55 when an injection of tetracyline was given. The injection was repeated after twelve hours. Within 24 hours the patient's temperature came down to normal (Fig. 2) although he still looked mentally confused.

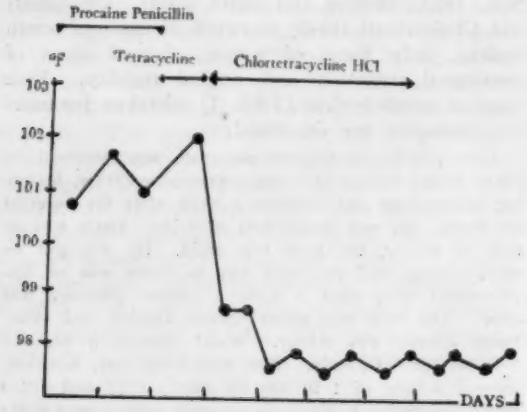

FIG. 2—SHOWING RESPONSE TO ANTIBIOTICS (CASE 2).

He was put on aureomycin 250 mg. eight hourly. He improved steadily. On 22-9-55, i.e., on the 17th day of his illness Widal and Weil-Felix tests were done, the results of which are shown in Table 1.

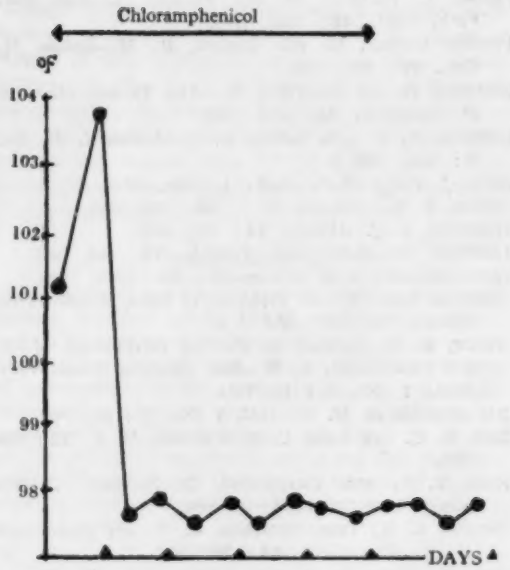

FIG 3—SHOWING RESPONSE TO ANTIBIOTICS (CASE 3).

Case 3—B.R., a twenty year old female, was admitted on 27-10-55 with a history of 12 days' continuous fever. The fever had come with chill and she had also complained of headache, later on she became delirious. On examination she was semiconscious, looked apathe-

TABLE 1—SHOWING CLINICAL FEATURES AND LABORATORY FINDINGS OF THE REPORTED CASES

Case No., Age & Sex	Duration of fever in days	State of consciousness	Rash / Eschar	W.B.C./ c.mm.	Poly (per cent)	Mono (per cent)	Lympho (per cent)	Widal	Weil-Felix (OXN)	Neck rigidity / Kernig's sign	Result
1 55 M	11	Unconscious	Nil	10,500	88	12	—	1 in 50	1 in 500 titre rose to 1 in 1250	Rigid / Positive	Cured with chloramphenicol
2 35 M	14	Dull	Nil	10,300	93	4	—	Negative	1 in 250	Slight / Negative	Cured with tetracycline
3 20 F	12	Semi-conscious	Nil	4,000	38	48	14	1 in 50	1 in 250 rose to 1 in 800	Slight / Negative	Cured with chloramphenicol
4 30 M	15	Dull	Nil / Eschar	6,000	76	24	—	Negative	1 in 250	Slight / Negative	Cured with chloramphenicol
5 35 M	14	Dull and apathetic	Rash / Eschar	4,300	64	36	—	Negative	Negative later positive 1 in 160	Rigid / Positive	Prompt response to chloramphenicol and cured

N.B.—C.S.F. normal in all the cases.

tic and dull. The spleen was soft and was enlarged one finger below the costal margin. Rhonchi and crepitations were present in both the lungs. The neck was slightly rigid. Results of examination of blood are shown in Table 1. The Weil-Felix titre 2 days later rose to 1 in 800. Even before the result of the first Weil-Felix test was received she was suspected to be suffering from scrub typhus and was put on chloramphenicol 250 mg. four hourly. Her temperature fell from 103·8°F to normal 12 hours after the administration of the drug (Fig. 3). She gradually regained consciousness and was discharged cured. Altogether 4·5 g. of the drug was given to her.

Case 4—T.S., a thirty year old farmer, was admitted on 22-9-55 with a temperature of 104°F in a dazed condition. His neck was slightly rigid and the eyes were congested. Examination of the lungs showed both rhonchi and crepitations. He had an eschar on the right side of the chest below the axilla. He was diagnosed to be suffering from scrub typhus and was put on chloramphenicol 250 mg. six hourly. Inspite of the temperature becoming normal ((Fig. 4) after 24 hours

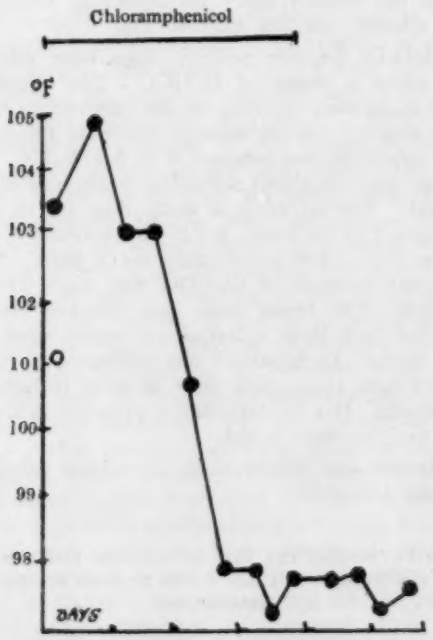

FIG. 4—SHOWING RESPONSE TO ANTIBIOTICS (CASE 4).

the patient remained a little dazed. His sensorium cleared gradually and he was discharged cured. He was given a total dose of 4 g. of the drug.

Case 5—P.D., a 35 year old male, had on 22-8-54 a rise of temperature with a chill which increased in intensity and soon became continuous; on the 5th day an erythematous rash was noticed all over his body but more marked on the abdomen and the back. He complained of severe headache and became drowsy. The state of his consciousness deteriorated and he was admitted to the Civil Hospital, Karnal, on 5-9-54. On examination his neck was rigid, the spleen was enlarged 2 fingers below the costal margin and was firm. The inguinal glands on both the sides were enlarged and a necrotic ulcer was seen in the lumbar region of his back in the middle line. The rash was fading. On the strength of our previous experience and without waiting for the result of the serological tests we decided to treat the case as one of scrub typhus. He was put on chloramphenicol 250 mg. four hourly. It had a remarkable effect, the patient regained consciousness after 24 hours and the temperature also fell to 100·6°F. After 36 hours the temperature became normal and the patient made an uneventful recovery. The first Widal and Weil-Felix tests were negative but when repeated 20 days after the onset of the fever the Widal was found to be negative, but the Weil-Felix test was positive with a titre of 1 in 160 for OXK.

Two patients admitted in an unconscious state, with rigidity of the neck, had positive Weil-Felix test for OXK. No antibiotics could be administered and both died.

DISCUSSION

The diagnosis was made on the clinical condition of the patient, positive Weil-Felix test and negative findings in the cerebrospinal fluid. In Cases 1, 3 and 5 there was a rising titre for OXK. In Cases 2 and 5 only a single Weil-Felix test could be done, but in all of them the titre of OXK was 1 in 250. In none of the cases was the titre of OXK less than 1 in 250. According to Krishnan *et al* (1949) 90 per cent cases of scrub typhus show a titre of 1 in 125 to 1 in 250 and only 10 per cent show a titre above 1 in 500. In Case 5 a titre of 1 in 160 was reached on the 20th day, previous to this he had shown a negative reaction to OXK and before the 20th day it was difficult to say with certainty that he was a case of scrub typhus. Such cases of scrub typhus and others who show a negative Weil Felix test may be missed and die unless they are treated with antibiotics known to be useful in the treatment of the disease. All the cases were serious. In Case 1 the drug was withdrawn early and he got a relapse which was controlled by the re-administration of the antibiotics. Cases which received penicillin and sulphadiazine under a wrong provisional diagnosis of meningitis did not respond to the treatment. Of the five cases, two had an increase of polymorphs. Such a thing may happen in some cases of scrub typhus. Case 5 showed increased monocytosis which occurs in some cases of typhus. The cerebrospinal fluid was normal in all the cases. All the cases except one came from the rural areas. Eschar was noticed in Cases 4 and 5. These are the only cases of scrub typhus in Karnal in whom

an eschar has so far been found. Only one case (Case 5) showed rash. Krishnan *et al* (*loc. cit.*) have reported rash in only 20 per cent of all their cases of scrub typhus.

SUMMARY

Results of treatment with antibiotics in five cases of scrub typhus who got admitted to the hospitals in Karnal are reported. In areas where there is possibility of the occurrence of scrub typhus the disease must be differentiated from cerebrospinal and enteric fevers. Treatment in such cases should not be withheld because of the grave prognosis and must be given soon after the blood has been obtained for culture and serological tests. The drugs of choice being chloramphenicol, chlortetracycline, oxytetracycline or tetratcycline and not penicillin and sulphadiazine which are not effective in scrub typhus but are usually given under a mistaken diagnosis of meningitis.

ACKNOWLEDGMENTS

Our thanks are due to the Director of Health Services, Punjab, for allowing us to publish this paper and to Dr. Nirmal Prakash, Civil Surgeon, Karnal for permitting us to use hospital records.

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A PRELIMINARY STUDY ON THE TREATMENT OF MALARIA WITH QUININE-CALCIUM GLUCONOGALACTOGLUCONATE

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In an earlier experimental study on the toxicity of quinine-calcium gluconogalactogluconate (QCGGG) on the cardiovascular system of dogs, it was demonstrated that QCGGG is a much safer drug when administered parenterally as compared with quinine (Jindal, 1955). Encouraged with this experimental study in dogs, a clinical study of about 40 established cases of malaria was undertaken with a view to find out the efficacy of QCGGG in human malaria and its toxicity, if any, on parenteral administration.

Similar work has already been done chiefly by Perret-Gentil (1956) who made an extensive study of QCGGG injections in the treatment of malaria. He has tried QCGGG injections in 38 patients who received altogether over 500 injections of QCGGG by the intravenous route. Not the slightest accident or untoward reaction has been reported. It was found that QCGGG alone can stop the development of a malignant tertian attack and lead to defervescence. The parasites disappear from the circulating blood on the second or the third day or in exceptionally severe cases on the fifth day. Similar observation has been made by Salgodo (1946) who has 'treated hundreds of malaria cases with QCGGG with excellent results'.

In the present study the following procedure was adopted for the clinical trial :

Malarial parasite positive cases were selected and given a course of QCGGG. The injections were given each morning by the intravenous route very slowly. On an average the time taken for each injection was between 4 to 5 minutes. The dosage was calculated according to the age of the patient. For an adult a daily dose of 10 c.c., between 7 to 15 years, 5 c.c. and between 4 to 7 years, 2 c.c. was given daily for 4 days. A 10 per cent solution of QCGGG was used without dilution. The blood films were checked on the 4th day and then subsequently every week for four weeks. Each patient was instructed to report at any time there were signs of fever in between the weeks. Day to day clinical progress, reactions and toxicity were noted.

Results and observations have been tabulated (Tables 1 and 2).

TABLE 1—SHOWING THE TYPE OF MALARIAL INFECTION AND THE NUMBER OF CASES WHICH SHOWED SPLENIC ENLARGEMENT

Type of malarial parasite	No. of cases treated	No. of cases with splenic enlargement
Benign tertian ...	13	5
Malignant tertian ...	23	16
Mixed (B.T. and M.T.) ...	4	2

TABLE 2—SHOWING THE ANALYSIS OF THE RESULTS AFTER THE QCGGG TREATMENT

	Benign tertian		Malignant tertian		Mixed infection	
	No.	%	No.	%	No.	%
Apyrexial						
1st day ...	12	92·0	19	82·6	2	50·0
2nd day ...	1	7·6	3	13·0	2	50·0
3rd day ...	—	—	1	4·0	—	—
Spleen regression ...	4	80·0	14	60·7	2	100
Side effects:						
Nausea, vomiting and diarrhoea ...	1	7·6	1	4·3		
Giddiness ...	1	7·6	2	8·6		
Relapses ...	2	15·2	6	25·8	2	50·0

It is quite evident from Tables 1 and 2 that there have been from slight to nil reaction in most of the cases. The slight reactions have been in the nature of nausea, vomiting and giddiness immediately after the injections. There was no appreciable change in the pulse or blood pressure which was constantly watched in all the cases. Regarding the clinical efficacy most of the patients became afebrile after the first injection except seven out of forty that is 17 per cent which became afebrile after the second injection. Relapses were high as seen in 10 out of 40 cases that is 25 per cent which had to be administered a second or third course of QCGGG injection. The relapses occurred at different times varying from one week to four weeks after the conclusion of the 4 day treatment. The enlargement of the spleen varied from just palpable to three fingers below the costal margin. The spleen regressed in 21 cases within four days to two weeks. A course of QCGGG consisted of 4 injections in most of the cases except in those cases which showed relapses. Blood films were negative after the course of QCGGG injections except for the gametocytes which persisted or appeared after the course of QCGGG injections, showing thereby that the drug has no action on the gametocytes.

SUMMARY

1. In the present study with QCGGG clinical cure has been attained in 75 per cent of cases while relapses have been seen in 25 per cent of cases.

2. QCGGG has been found effective against B.T. and M.T. type of parasites but ineffective against their gametocytes.

3. The drug is not meant for routine treatment of malaria.

ACKNOWLEDGMENT

The author is grateful to Dr. N. Tyagi, Honorary Pathologist, District Hospital, Muzaffarnagar, for blood film examination of the cases under review. The author is thankful to Messrs. Sandoz Products Ltd., for a liberal supply of Calgluquine (Quinine-calcium gluconogalactogluconate) for clinical trial.

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COMPLEMENT VALUES IN EXPERIMENTALLY INDUCED DEFICIENCY STATES IN GUINEA PIGS

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AND

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Complement, one of the essential factors in antigen-antibody reactions, is normally present in the sera of all men and animals. Its activity varies widely in the sera of different species and equally strikingly in the same species. Amongst all laboratory animals, guinea pig serum contains complement of the highest concentration and constancy.

Numerous views have been put forward regarding the origin and chemistry of complement and the many factors influencing compiement activity of sera have been studied experimentally, in the past. Ecker *et al* (1938) and Chu and Chow (1938) concluded that in guinea pigs, complement values depended directly on serum ascorbic acid concentration whilst Spink *et al* (1942) found no such relationship.

The low complement values observed in guinea pigs, during winter months, have been attributed by some workers to a dietetic deficiency associated with a lack of green food but there have been very few experimental publications correlating complement values with vitamin A content of blood. The effect of protein deficiency on complement has likewise received very little attention.

The present study has been undertaken to investigate the effect of deprivation in diets of (i) vitamin A and (ii) methionine and cystine.

TABLE 1—SHOWING DIETS GIVEN, AVERAGE SERUM VITAMIN CONTENTS AND AVERAGE COMPLEMENT VALUES

Diet	1st day		10th day		20th day	
	Vitamin	Complement	Vitamin	Complement	Vitamin	Complement
Devoid of vitamin A ...	100 units %	48·33	20 units %	50·0	not done	54·0
Devoid of vitamin C ...	2·3 mg. %	40·0	1·3 mg. %	71·0	1·8 mg. %	62·0
Balanced	—	50·0	—	65·0	—	56·66

TABLE 2—SHOWING AVERAGE COMPLEMENT VALUES WITH A METHIONINE AND CYSTINE EXCLUDED DIET

Nature of animals	1st day	10th day	20th day	30th day	40th day
Experimental	66·66	66·66	51·7	45·0	30·0
Control	50·0	65·0	56·66	74·0	60·0

The controversial role of vitamin C in complement values has also been re-examined.

MATERIAL AND METHODS

Three groups of 6 guinea pigs each (groups 1, 2 and 3) were employed in the experiment and one group of 8 animals served as the control (group 4). Groups 1, 2 and 3 were maintained on diets devoid of vitamin A, methionine and cystine and vitamin C respectively (Schedules A, B and C). The control group was maintained on a balanced synthetic diet (Schedule D). All the animals were bled consecutively at 10 day intervals and the serum complement values estimated as also the vitamin A and vitamin C contents in groups 1 and 3 respectively. Because of the poor condition of the animals, the experiments relating to groups 1 and 3 were terminated after three weeks while with group 2, it was possible to continue the experiment for 6 weeks.

Complement was estimated in terms of its haemolytic activity against a 3 per cent suspension of sensitised sheep red cells. The highest dilution of the serum causing complete haemolysis of sensitised sheep red cells, after incubation at 37°C for half an hour, was regarded as the complement titre and the reciprocal of this was designated as the complement value.

Vitamin A content of sera was estimated by the modified method of Pett and Lepage (1940) and vitamin C by the technique of Mindlin and Butler (1938).

RESULTS

The results are recorded in Tables 1 and 2.

Elimination of vitamin A from the diet caused a lowering of serum vitamin A content but there was no corresponding alteration in complement values.

Deprivation of methionine and cystine caused a gradual but definite fall in complement values.

Deprivation of vitamin C influenced serum ascorbic acid levels to a minor degree but did not lower complement values.

The fluctuation in complement values observed in vitamin A and vitamin C deprivations does not appear significant, since it was also noted in control animals maintained on balanced diet.

COMMENTS

The essential role of complement in antigen-antibody reactions, though disputed earlier by Dale (1913), is now an accepted fact. Complement thus assumes an important place in humoral immunity and its quantitative variation in the sera of individuals should cause corresponding alteration in their immunity to infection.

Several other factors, such as vitamin deficiencies, disordered nutrition and certain diseases have been independently correlated with diminution of immunity to disease and it is but natural that efforts should be directed towards understanding the relationship, if any, between such factors and complement.

Vitamin A has for long been described as an anti-infective vitamin, supposed to help resistance to infection by direct participation in immunological reactions. However, since Wolbach and Howe (1926) demonstrated widespread epithelial atrophy

followed by squamous metaplasia and keratinisation, in vitamin A deficient animals, it has been generally accepted that vitamin A plays its anti-infective role only through its ability to maintain epithelial integrity.

The results of the present experiment, i.e., the gross reduction in serum vitamin A content of guinea pigs maintained on vitamin A deprived diet, with no corresponding alteration in serum complement values, would appear to prove that vitamin A deficiency does not alter the level of immunity through its effect on serum complement.

The gradual but definite fall in complement values on a diet deprived of methionine and cystine is interesting, particularly since the amino acids in question are known to be "liver protective" in nature. This would be in keeping with the observations of Ehrlich and Morgenroth (1900) and Dick (1913) who demonstrated a reduction in complement values of rabbits receiving hepato-toxins.

Is it likely then that serum complement activity is related to liver integrity? Is its reduction in disease and malnutrition with the resultant lowering of resistance to infection, directly attributable to hepatic damage? Our own observations in further experiments, to be published, indeed point in this direction.

Deficiency of ascorbic acid in animals and human beings has been observed to impair their defensive reaction to infection. Many attempts have been made to correlate this anti-infective activity more specifically with factors participating in immunological reactions. Conflicting views have been held by workers, regarding the relationship between complement activity and serum ascorbic acid levels, some noting a significant alteration in the former with a change in the latter and others refuting any such connection.

Our own results would indicate that it is doubtful if complement activity is at all influenced by deprivation of ascorbic acid. As such, the anti-infective activity of ascorbic acid would not appear to be achieved through complement.

Summary

Complement values in 26 guinea pigs (including controls) subjected to deprivation of vitamin A, methionine and cystine, and vitamin C, have been estimated.

Deprivation of vitamin A in diet, caused lowering of its serum content but no corresponding change in the complement.

Exclusion of methionine and cystine produced a gradual but definite fall in complement values. A suggestion is made that this is due to hepatic damage.

Deprivation of vitamin C caused no alteration in serum complement.

It is concluded that the anti-infective activity of vitamin C, observed by previous workers, is not achieved through complement.

DIET SCHEDULES A, B, C AND D

Showing Relative Proportions of the Constituents

Constituents	Sch. A	Sch. B	Sch. C	Sch. D
Starch	50·0%	50·0%	50·0%	50·0%
Sucrose	25·0%	25·0%	25·0%	25·0%
Olive oil	4·0%	4·0%	4·0%	4·0%
Casein hydrolysate	14·0%	14·0%	14·0%	14·0%
Tryptophane ...	0·34%	0·34%	0·34%	0·34%
Cystine	0·33%	0·0%	0·33%	0·33%
Methionine ...	0·33%	0·0%	0·33%	0·33%
Salt mixture ...	2·0%	2·0%	2·0%	2·0%
Yeast	4·0%	4·0%	4·0%	4·0%
Vitamin D ...	300 units	300 units	300 units	300 units
Vitamin C ...	15 „	15 „	0 „	15 „
Vitamin A ...	0 „	30 „	30 „	30 „

N.B.—All the animals were allowed to feed *ad lib.*

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CASE NOTES

NEUROMYELITIS OPTICA WITH XANTHOCHROMIA OF CEREBROSPINAL FLUID

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Since the publication of the full description of a case of neuromyelitis optica by Erb in 1879 over two hundred of such cases have been reported from several parts of the world. Five cases have been reported so far from India. McIntyre and McIntyre from America reported for the first time in 1952 three cases of neuromyelitis optica with xanthochromia and spinal block. As far as we can see a similar case has not been reported from India.

CASE REPORT

M. I., Muslim male, aged 42, a tailor, was admitted into the hospital on 30-1-56 for difficulty of breathing, paraplegia and loss of vision in both eyes. The illness started 7 weeks ago with fever lasting for 2-3 days. This was followed 2-3 days later by pain in the back and waist with weakness in the lower limbs. He developed sensory loss in the lower half of the body and difficulty in passing urine and stools after 4 weeks from the onset. A fortnight later he noticed dimness of vision in both eyes. Condition becoming aggravated he got himself admitted in a hospital where suprapubic cystostomy was done.

Past illness, family history and personal history were of no significance.

Nervous system—On examination all the cranial nerves were normal, except the optic (described later). There was complete loss of power in both the lower limbs with flaccid type of paralysis, and moderate loss of power in both the upper limbs with spasticity. All varieties of skin sensations were absent upto the level of the 3rd intercostal space. The deep reflexes of the lower limbs were lost. The biceps jerk was exaggerated on both sides. Both plantar and abdominal reflexes were absent. There was no control over the movement of the bowels.

Examination of eyes showed that in both the eyes there was no perception of light. Pupils were dilated and not reacting to light. Movements were normal in all directions but painful. Fundii oculi showed optic neuritis with 2 dioptres of swelling of the disc.

The diaphragm was very weakly acting and the intercostal muscles not at all acting. Other systems were normal.

Laboratory investigations—Haemoglobin 10 g. per cent. R.B.C.—4·5 million per c.mm., W.B.C. 12,000 per c.mm. with neutrophils 75 per cent, lymphocytes 24 per cent, and eosinophils 1 per cent. W.R. was negative. Urea 45 mg. and N.P.N. 39 mg. per 100 c.c. respectively.

The cerebrospinal fluids was clear and yellow with a normal rate of flow. Sugar—36 mg., chloride—640 mg., protein—950 mg. per 100 c.c. respectively. Lymphocytes—12 per c.mm. W.R. was negative. Langes colloidal gold reaction—paretic type (55543200000).

Stools and urine—No abnormality was present.

The patient had a rise of temperature ranging between 99° and 101°F for 4 days after admission. There was progressive development of paralysis of both the upper limbs, dysarthria, dysphagia and bed sores over pressure points. He died of respiratory failure due to ascending paralysis on the 18th day after admission. He was kept in iron lung throughout his stay in the hospital.

DISCUSSION

Myelitis and optic neuritis in a middle aged man of 42 and the fatal termination due to the ascending nature of the paralysis conform to the diagnosis of neuromyelitis optica.

The interesting feature of this case is the presence of xanthochromia with high protein content of the C.S.F.

In two of the cases reported by McIntyre and McIntyre (1952) xanthochromia was due to spinal block resulting from cystic adhesive arachnoiditis proved by laminectomy. Our case is similar to those reported by McIntyre and McIntyre (*loc. cit.*) so far as xanthochromia is concerned. The patient's general condition did not allow further investigations.

SUMMARY

A case of neuromyelitis optica with xanthochromia of the cerebrospinal fluid is reported.

ACKNOWLEDGMENT

Our thanks are due to Dr. M. N. Sarkar, the Principal and Superintendent, Medical College Hospitals, Calcutta for his kind permission to publish the case records.

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THE PROBLEM OF ACUTE PYOGENIC INFECTION IN PATIENTS HYPERSENSITIVE TO PENICILLIN

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INTRODUCTION

With the advent of penicillin, acute infections caused by gram-positive organisms have lost much of their virulence. Toxic reactions are few and far between, thus enabling us to take advantage of this widely employed antibiotic in our everyday practice. Hypersensitivity to penicillin was observed in a case where, but for the drug allergy, the treatment would have been very simple. The case is reported.

CASE REPORT

B. L., a male aged 35 years, had a small boil just below the angle of the right mandible, without any constitutional disturbances. On 10-5-56 the patient himself while palpating it inadvertently squeezed the nodule. This resulted in rapid spread of the infection and on the next morning he noticed the inflamed area pointing at multiple heads. There was fever and anorexia and on 12-5-56 the pain increased. On the same day the patient presented himself before a doctor who advised injection of procaine penicillin, magnesium sulphate compress and a sulpha drug. He took the sulpha tablets as directed and only one injection of procaine penicillin. Soon after the injection he developed generalised itching which gradually increased in severity till 22-5-56 when the whole body was covered with urticaria-like rash. Blood and urine examination did not reveal any abnormality, Wassermann and Kahn tests were negative.

It was thought that the patient was hypersensitive to penicillin and as such he had developed drug allergy. Different varieties of anti-allergic drugs were given by oral and parenteral routes and external application of soothing antihistaminic creams. This treatment was continued for three days without bringing much relief to the patient. On 26-5-56 procaineamide hydrochloride tablets 0·25 g. every 6 hours were administered orally along with the usual anti-allergic drugs. Within two days there was subsidence of the rash as well as symptomatic relief from itching which was hitherto unbearable.

On 2-6-56 another red tender nodule appeared just below the lower lip on the right side. Hot boric compress was applied but on 4-6-56 an indurated area of one inch diameter developed at that particular site. The regional lymph nodes were enlarged and there were constitutional symptoms. Chloramphenicol 250 mg. 6-hourly was orally administered for 2 days but the swelling was progressing.

On 6-6-56 the whole lower lip, chin and submental region became involved in the swelling with rise of temperature to 101°F. Chlortetracycline hydrochlor 250 mg. was given every 6 hours but even after 1 g. the effect was below expectation. The temperature went upto 103°F, P/R was 120/24 and the pain was excruciating. An injection of penicillin was fraught with the risk of drug allergy and withholding of the injection meant free allowance to cellulitis of the lower lip to extend its limits ushering in a grave prognosis. The decision was taken in favour of the former and five lac units crystalline penicillin was injected in preference to any combination with procaine for two reasons, viz., (i) to reach a high blood level rapidly as demanded by the severity of the infection and (ii) to avert the presumed toxic reaction to procaine penicillin.

On 7-6-56 the inflammation had greatly subsided but there was recurrence of itching all over the body. The temperature remained between 100 and 101°F. and the patient was very uncomfortable. Chlortetracycline capsules were continued along with alkalies, antihistaminics, calcium and vitamin C. Free flow of urine and daily clearance of bowels were arranged for.

On 9-6-56 there was no trace of inflammation in the lower lip but the trunk and upper limbs were covered with very big urticarial rashes together with swelling of eye-lids and forehead.

On 11-6-56 in the morning the face was very much swollen and the patient complained of a feeling as if the face and scalp would burst out. This swelling was distinctly non-inflammatory but angioneurotic. Anti-allergic drug was administered parenterally in addition to the oral route continued so long. In the evening the eyes could be opened and the swelling was less but still alarming.

On 12-6-56 procaineamide hydrochloride tablets were again started in combination with another antiallergic agent and within two days the patient became completely free from any illness after suffering for a month or so.

SUMMARY

A case hypersensitive to penicillin and not responding to anti-allergic agents is reported.

The use of procaineamide hydrochloride gave very good results.

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CALCUTTA, SEPTEMBER 16, 1956

TROPICAL EOSINOPHILIA AND PARASITISM

Long before the enunciation of Loeffler's[1] syndrome in 1932, and Weingarten's[2] description of tropical eosinophilia in 1943, the first pointer towards the pulmonary involvement in allergic disease came from Sir William Osler[3] and a few sporadic case reports[4, 5] marked the period in between. The recognition of the clinical condition resembling tropical eosinophilia and its response to arsenic was perhaps from the pioneer observations of Roy and Basu[6] for the first time in India in 1918. It is however, Frimodt-Möller and Barton[7] who are credited with the first description of the clinical condition, whereas Weingarten's[2] real achievement lies in putting the treatment on a rational basis. In spite of the wide acceptance of the term 'tropical eosinophilia' since then, it should be admitted that it is far from a happy and accurate one, if not misnomer, as eosinophilia is commonly associated with a host of other tropical conditions. Besides, increasing records of atypical cases with bizarre or protean manifestations seem to justify a change in the original concept of the clinical entity. The term pulmonary eosinophilia[8] was suggested for the whole group. Ball[9] was in favour of adding the word "pulmonary" to tropical eosinophilia, and using the term pulmonary infiltration with eosinophilia[10] (PIE syndrome) was conceived to have a descriptive appeal. "It would appear that many diseases manifesting eosinophilia and transitory lung changes are related, and form narrow bands on a broad spectrum with asymptomatic Loeffler's syndrome at one end and deadly periarteritis nodosa at the other"[11].

All these controversies and difficulties about the selection of an appropriate term for the clinical entity, however, owe their origin to the aetiological background of the disease, which is still shrouded in a thick mist of obscurity and confusion, successfully eluding the grasp of many a vigorous effort. Failure to incriminate the definite pathogen conclusively has resulted in the postulation of a number of theories about its aetiology.

Chaudhuri *et al*[12] gave an exhaustive account of the probable aetiological factors with a large number of references. This subject has kept the workers in different parts of the world busy with the task of accumulating evidences in support of each of the two broadly classified theories, allergic and infective. The former, however, seems to have come to steal a march in the race in recent years. Some were of opinion that the stimulating, sensitising, and aggravating antigen varies, but the condition is often cast in the mould of an allergic past[9]. The hypothesis that the condition of tropical eosinophilia is essentially an allergic one has also investigational support[12a]. Though the quest about the identification of the specific allergen is yet to be called a success, the parasitic role in the aetiology of tropical eosinophilia has been increasingly gaining ground in recent years. Parasitic or more precisely speaking, helminthic eosinophilia (because, protozoal eosinophilia is too insignificant to deserve any mention with a possible exception in amoebic infection, which too hardly merits a place in the context) in infection with parasitic helminths, e.g., *Ascaris lumbricoides*, *Strongyloides stercoralis*, *Trichinella spiralis*, *Trichuris trichura*, filarid parasites, hookworms, schistosomes, etc., is well recognised. What is required to be known is its relationship with the so-called tropical eosinophilia.

An investigation[13] revealed an intestinal or systemic helminthiasis in every one of 21 patients with massive eosinophilia. During this work, involving many thousands of haemograms, the workers failed to find one single case of 'essential eosinophilia', and they are of opinion that if such do occur in the tropics in the absence of parasites, and are in fact of any other origin, they are so exceptional that the words 'tropical eosinophilia'

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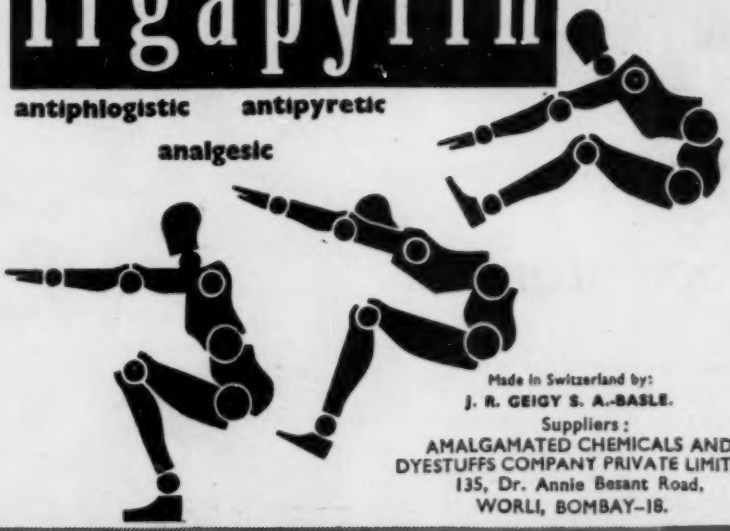

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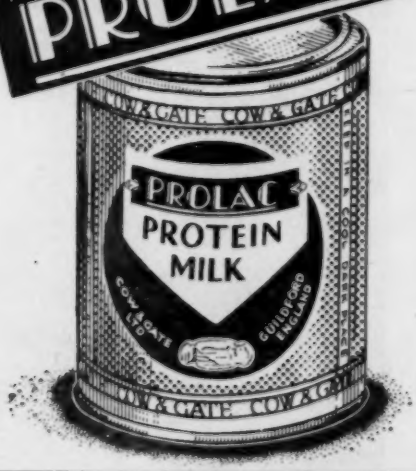

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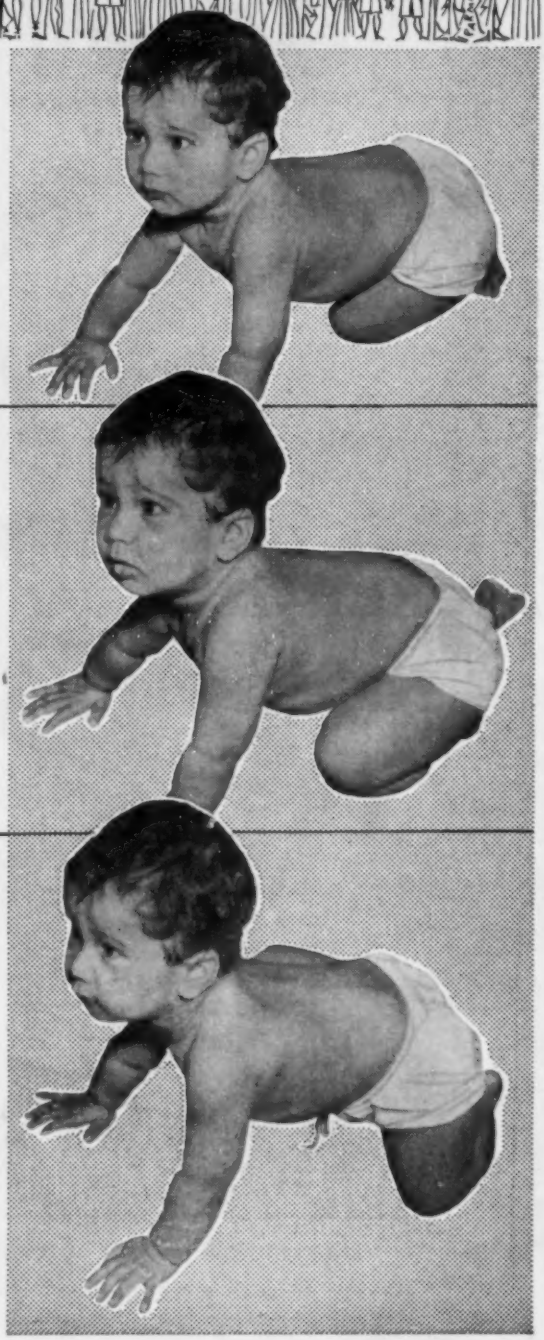

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can be erased from the vocabulary. Forty-three cases designated as tropical eosinophilia were investigated of which thirty-one had demonstrable parasitic infestation[14]. *Microfilaria malayi* was found in the excised lymph glands[15] from 7 out of 8 patients, whose blood did not show any microfilaria, and who were suffering from a syndrome characterised by superficial adenopathy, eosinophilia and bronchitis. It was considered that filarial infection might be an important if not the only cause of tropical eosinophilia. Filariasis is characterised by the persistence of eosinophilia at a high level for years even without inflammatory crisis, and the phenomenon of tissue eosinophilia, characterised by thrombosis and infiltration of the vascular walls and often formation of eosinophilic abscesses, is due to an acute allergic reaction, determined by the disintegration of the worm in hypersensitised persons[16]. It is further stated that filarial eosinophilia is sometimes accompanied by bronchopneumonic syndrome, like asthma, and is of allergic origin. While pointing towards the parasitic aetiology of tropical eosinophilia it was noted that in at least two out of the three patients the classical features of tropical eosinophilia were of filarial origin[17]. Microfilaria was found from the lymph glands of patients suffering from tropical eosinophilia[18, 19, 20, 21], and it was suggested[21] that what is usually known as tropical eosinophilia may be regarded as an accentuated state of sensitivity in persons predisposed by filarial infection.

Similarly numerous references are available about the pulmonary ascariasis with eosinophilia[10, 22, 23-29].

With an interesting experiment clinical deductions were formulated from 50 cases of induced ancylostomiasis[30]. It was observed that eosinophil curve increased rapidly reaching a peak of 50 to 75 per cent by the end of the 3rd month and falls as rapidly to 15 per cent by the end of one year. It was further commented that clinical study of ancylostomiasis in a tropical country is complicated by the presence of other infection and dietary deficiencies.

A number of other helminthic parasites similarly have been associated with the condition resembling tropical eosinophilia. Visceral larva migrans, in recent years, has received the recognition of a clinical entity[31, 32], characterised by chronic hypereosinophilia, pulmonary infiltration, hepatomegaly, fever, cough and hyperglobinaemia. This condition has been known to be due to invasion by the nematode larvae of the species *Toxocara canis* and *Toxocara cati*, for whom man is not the natural host[32, 33]. While making a "comparative study of hypereosinophilia in relation to aetiology", it was observed[34] that hypereosinophilia of more than 20 per cent is mostly due to parasitic infections and that not due to parasitic infection is usually under 20 per cent with the exception like tropical eosinophilia which, he thinks, may be due to some unknown parasitic infection.

Elsewhere in the current issue of this journal a pointed reference to the possibility of parasitism as an important factor in the aetiology of tropical eosinophilia has been made[35]. Cogent arguments have been advanced in favour of this proposition. It has been further advocated with sound reasoning that the allergic basis is an associated factor in the aetiology of the condition.

The nature of the reaction following a parasitic assault, its frequency and intensity, evolution and course depends upon factors such as intensity or amount of infestation, host responsiveness and tolerance, the speed and duration of invasion and above all the association of any other pre-existing or concomitant conditions. The resultant tissue

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damage may, therefore, vary from a transient, ill-appreciable, reversible one to the gross well-pronounced morbid changes leading to an acute or chronic well-established clinical entity. The extreme variability in the clinical course of the disease, tropical eosinophilia, with preponderance of one or more of the so-called cardinal features, therefore, can reasonably be attributed to the relative activities of one or more of the factors, governing the ultimate outcome of the infestation.

It has been a well-recognised fact supported by the clinical and experimental observations that eosinophilogenic response to the parasitic stimulus is not uniform all through the course of the disease, depending on a number of factors such as degree of sensitisation, adrenocortical activity, etc. That the hypereosinophilia due to parasitic infections is characterised by the regularity with which it is produced by the exciting agent has been observed[12]. Polyparasitism at times is believed to exhaust the eosinophilogenic reacting power of the body. Possible association of eosinopenic factors, e.g., acute infection or otherwise is also a likely event. So absence of uniform and persistent hypereosinophilia in the parasitic infestation cannot with justification be offered as an argument against their causal relationship.

Failure to demonstrate any laboratory evidence of parasitic infestation in all the cases has also been advanced to rule out the parasitic role in the production of tropical eosinophilia. Besides the technical errors, which are by no means uncommon in the detection of helminthic ova in stools, the pulmonary excursion of the parasitic helminths with the resultant eosinophilia is mostly an event of the larval stage occurring long before the worms are in the reproductive age to produce demonstrable eggs. Hence eosinophilic response and the egg production may not run *pari passu*. It is no wonder that absence of persistent and careful laboratory investigations for a prolonged period has to some extent been responsible for the denial of parasitic contribution in the causation of tropical eosinophilia. Microfilariaemia, again a reputed illusive phase of filarial infection, is encountered in a very small percentage of filarial subjects. Needless to mention that a diagnosis of the disease filariasis can ill-afford to depend only on the state of demonstrable microfilariaemia.

It is obvious that negative laboratory evidence does not hold as much value to deny the parasitic infestation, as the positive one does in establishing the same. It has been rightly pointed out[35] that failure to demonstrate the laboratory evidence of parasitic infestation cannot definitely invalidate the parasitic role in tropical eosinophilia.

That parasitic worms or their emanations may sensitise an individual to produce a syndrome resembling tropical eosinophilia has been admitted[36] but such parasitic infections occur more frequently in the tropics than tropical eosinophilia. These observations, however, only serve to indicate that all parasitic infections do not inevitably result in tropical eosinophilia. This does not take away the potentiality of parasitic infection to cause tropical eosinophilia.

Above all the accidental human infection by abnormal helminthic parasites as in visceral larva migrans stated before, is also a quite like occurrence, when man being the inappropriate host, attempt for diagnosis by ordinary laboratory methods is bound to be a failure.

The remedies employed in tropical eosinophilia seem to bear an additional testimony to the probable parasitic aetiology of the disease. The therapeutic efficacy of arsenic in parasitic infections like filariasis, amoebiasis, etc., is well-known. It has already been suggested that the therapeutic response to arsenic in tropical eosinophilia is attributable to its action against some parasitic pathogen, yet to be identified decisively. Diethylcarbamazine recently used in tropical eosinophilia[35, 37] probably exerts its beneficial effect by virtue of its well-recognised anthelmintic property. This drug, however, has also been used on earlier instances with a remarkable success on filarial patients with classical features of tropical eosinophilia[15, 17].

Hence parasitism appears to play a distinct and significant role in the aetiology of tropical eosinophilia. The fact that transfusion of 250 c.c. of blood from patients suffering from tropical eosinophilia failed to induce any recognisable change in any of the recipients[35] substantially undermines the possibility of any blood borne infection, bacterial or viral. It is, therefore, possibly an unholy combination of parasitism and the resultant allergy in response to it, that determines the aetiopathogenesis of the disease. The entire episode indeed may be conditioned by paroxysmal bouts of allergic disorder in response to some parasitic allergen.

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CURRENT MEDICAL LITERATURE

Hazards of Penicillin Therapy

RAJAM AND RANGIAH (*J. Indian M. Sc.*, **10** : 337, 1956) deal with penicillin reactions under the following different heads :

Serum sickness type of reaction is the commonest type of reaction met with in clinical practice and has definite incubation period occurring not earlier than five days or later than three weeks. The manifestations are pruritus, urticaria, joint pains, fever, lymphadenopathy and eosinophilia. The average duration of symptoms is ten days but may be prolonged to eight weeks or more. In exceptional cases, the serum sickness reaction may recur and last for a year. This type occurs most often after repository penicillin.

Anaphylactic shock—This reaction is at once, the most unpredictable, profound, dangerous and sometimes fatal of all the allergic reactions encountered following penicillin therapy. The reaction begins a few seconds or minutes after the injection. Premonitary symptoms of a peculiar taste in the mouth or sensation in the tongue, sneezing, or tingling in the extremities may or may not be noticed by the patients. These are followed with lightning rapidity by a severe constriction or pain over the chest or abdomen often with nausea or sudden desire to defaecate. A choking sensation in the throat and dyspnoea with cyanosis and frothy sputum occur simultaneously with symptoms of syncope, peripheral circulatory collapse, terminating in unconsciousness and even death. Fatal reactions rarely begin more than 15 minutes after the drug is administered.

Hyperergic Reactions—These reactions are of the delayed protracted type, and in many cases have resulted in death.

Exfoliative dermatitis—It is a delayed type of reaction commencing with a diffuse itchy rash. In severe cases, a fatal outcome may occur and autopsy has revealed vascular and visceral lesions in such cases. The exfoliative dermatitis may become haemorrhagic and gangrenous.

Bullous dermatitis—The type less common than exfoliative dermatitis, is a dangerous manifestation of penicillin sensitivity and is associated with severe systemic symptoms.

Purpuric reactions—These reactions may occur alone or in association with the severe type of exfoliative dermatitis. The purpuric lesions may be cutaneous, visceral or both.

Arthus or Schwartzman reactions—Clinically they are characterised by a local haemorrhagic necrotic reaction of the skin both at the site of penicillin injection as well as in other areas of the body. The pathogenesis is a necrotising arteritis and thrombophlebitis with haemorrhage resulting in localised necrosis of the epidermis and dermis.

Agranulocytosis—Agranulocytosis seems to be rare with penicillin.

Periarteritis nodosa—In prolonged drug sensitivity reactions, organic destructive vascular lesions may occur with widespread involvement of viscera and associated with renal, hepatic and myocardial changes.

Acute myocardial infarction—Though rare, reversible electrocardiographic changes have been reported with delayed and protracted penicillin reactions.

Fatal Jarisch Herxheimer reaction—This peculiar reaction occurs only in patients with syphilis treated with treponemicidal drugs. The reaction may be systemic and focal and comes on within six to twelve hours and lasts 12 to 24 hours. The focal component of the reaction is of some prognostic significance in late syphilis, particularly cardiovascular and neurosyphilis.

L. E. phenomenon—Penicillin allergy may play a possible aetiological role in some cases of lupus erythematosus disseminatus.

A solitary case of *acute yellow atrophy of the liver* following penicillin in a syphilitic patient has been reported. The occurrence of the condition is suggestive of an acute hepatic Herxheimer reaction.

Erythematovesicular eruption—It occurs as another form of generalised allergic reaction to penicillin. With a shorter incubation period than the urticarial reactions this tends to occur over the hands, feet and groins and subsides with a branny desquamation. The shock tissue is the epidermis, whereas in urticaria the shock tissue is the superficial part of the dermis.

Contact dermatitis—Contact dermatitis is a delayed type of sensitisation of skin and mucous membrane which occurs in patients treated with topical application of penicillin.

Other infrequent or rare reactions to penicillin—Loeffler's syndrome, has been reported in some cases after injection of penicillin in oil and beeswax. Philpott and coworkers reported on a patient who developed a *sarcoid-like granuloma* at the site of injection of penicillin. A rare complication in syphilitic patients treated with penicillin is *epididymitis*. Cases of *'black tongue'* have occurred after administration of penicillin as a troche.

The authors give below a course of treatment of penicillin reactions :

Anaphylactic shock : It is difficult to evaluate the treatment of this dangerous complication of penicillin therapy.

In the non-fatal cases the majority of the patients have recovered without any treatment. In others who have recovered after treatment the credit for recovery goes to the therapy employed. In many of the reported fatal cases death came on so quickly in about five to ten minutes that no treatment could be given. In others, in spite of energetic anti-anaphylactic measures, the patients died. But in spite of the unpredictability of the outcome of this deadly complication, prompt and energetic measures should be taken.

(a) Epinephrine subcutaneously, or intramuscularly (0·5 to 1 ml.) should be immediately given and repeated every few minutes as determined by the patient's condition. Failure to repeat the drug in the case reported by

Kern resulted in the return of the shock symptoms and death.

(b) A tourniquet should be applied proximal to the site of injection provided the injection had been given in the upper arm or lateral aspect of the thigh.

(c) Intravenous antihistamine may also be administered.

(d) The patient should be in the recumbent position and adequate airway should be maintained in the unconscious patient.

(e) Oxygen, if necessary under positive pressure, should be given in case of marked cyanosis and dyspnoea.

(f) In intractable penicillin shock lasting for some hours, Siegal recommends intravenous therapy with the most potent antishock remedy norepinephrine. Whole blood or plasma is also said to be valuable.

Serum sickness type of reaction and chronic urticaria : Antihistamines should be given in full dosage and gradually tapered off, if the symptoms are relieved. In intractable cases of urticaria, a cautious desensitisation with penicillin may be attempted.

In prolonged and serious penicilin reaction such as exfoliative dermatitis, periarteritis nodosa, cortisone in gradually stepped down doses should be administered sometimes for prolonged periods.

Utilization of Animal and Vegetable Protein

PHANSALKAR AND PATWARDHAN (*Indian J. M. Research*, **44** : 1, 1956) write :

Nitrogen metabolism was studied in young adult Indian male volunteers at levels of protein intake just sufficient to maintain N equilibrium. The sources of proteins were : (a) whole egg, (b) single cereal, such as wheat, and (c) a mixture of cereals and pulse in the respective experiments. Nearly 80 per cent of the total dietary N was derived from the test protein. The observations made and conclusions arrived at are given below :

1. Urinary N was higher on wheat alone than on whole egg, thereby throwing the body into negative N balance during wheat diet period. On the other hand, with a mixture of cereals and pulse urinary N was lower than on whole egg.

There were changes in faecal N which in many cases were unrelated to those occurring in urine N.

2. The observations on wheat protein confirm those reported by Murlin *et al* in American subjects showing that N metabolism in Indian subjects was strictly comparable with that in the American subjects who were habituated to a high level of N metabolism.

The biological and egg replacement values of vegetable protein were higher when the latter was derived from mixed cereals and pulse than when it was derived from a single cereal such as wheat.

. These experiments gave additional proof that pulses are good supplements to cereals in improving the quality of dietary protein.

The minimum level of protein intake required to maintain N equilibrium was calculated from the results obtained in these experiments and was found to be 3·55 g. N/sq. m. of body surface area. This value agrees fairly closely with the values reported in Western subjects by other workers referred to in the text.

Urinary Excretion of Pressor Amines

NATARAJAN AND OTHERS (*Indian J. M. Research*, **44** : 131, 1956) write.

Twenty-four-hour urinary excretion of pressor amines, in terms of adrenaline, has been estimated in sixty normal Indian subjects. The results have been statistically analysed and it has been found that no significant relationship exists between urinary excretion of pressor amines and height, weight and age either singly or in combination. Importance of establishing the limit of urinary excretion of pressor amines over which phaeochromocytoma will be indicated has been stressed.

Anaemia in Ankylostomiasis

DAFTARY AND BHENDE (*J. Postgraduate Med.*, **2** : 44, 1956) in reporting on the haematologic and other findings in a series of 96 cases of ankylostomiasis made the following observations :

Seventy four cases were anaemic and 22 non-anaemic.

Of the anaemic group, in 22 cases the marrow was megaloblastic; these, latter, were considered to be cases of nutritional megaloblastic anaemia complicated by hookworm infection.

In the remaining 52 cases the marrow was normoblastic. In this group the type of anaemia was microcytic in 23, normocytic in 21 and macrocytic in 8.

The severity of the anaemia was not related to the load of the parasite, as judged by the egg-count.

The pathogenesis of the anaemia is briefly discussed.

Depigmentation of Skin in Intestinal Parasitic and Bacterial Diseases

SAHU (*Indian Practitioner*, **8** : 119, 1955) gives below the summary of the clinical observations on the incidence of depigmentation of skin in intestinal parasitic and bacterial diseases :

For the last five years investigations are carried out on 621 patients suffering from depigmentation of skin-hypopigmented patches coming from different parts of the state of Orissa in the out-patient and in-patient departments of skin diseases of S. C. B. Medical College Hospital, Cuttack. Out of them 147 cases are of intestinal parasitic and bacterial diseases. The incidence of depigmentation of skin in :

Amoebiasis 31·5 per cent, giardiasis 15 per cent, ankylostomiasis 15·5 per cent and bacillary dysentery 13·5 per cent.

It has been observed by the author that the incidence of depigmentation of skin in children is specially due to chronic bacillary dysentery and giardiasis.

Motor Unit in Leprous Neuritis

DASTUR (*Neurology*, **4** : 1, 1956) in presenting a clinical and pathological study of the peripheral nerves, myoneural endings and striated muscle in leprous neuritis observes :

Both ulnar and lateral popliteal nerves were almost always affected : the thickening was not necessarily symmetrical.

Cutaneous insensibility in the upper extremity usually extended over the area of distribution of the ulnar nerve and the medial cutaneous nerve of the fore-arm, and sometimes over the areas of the median and radial nerves also.

Cutaneous insensibility in the lower extremity usually extended over the area of distribution of the lateral popliteal and anterior tibial nerves.

The zone of sensory loss was generally well defined and roughly corresponded to the anaesthetic areas resulting from peripheral nerve injuries.

In the majority of cases there was some correlation between sensory and motor impairment.

The motor power and function of at least one upper extremity were found unaffected in 17 cases.

The motor power and function were moderately affected in another 17 cases, where weakness of abduction and adduction, usually of the medial 2 fingers, was noticeable.

In 30 severely affected cases wasting of the intrinsic muscles of the hand with severe impairment of movement of the medial fingers, and frequently of the lateral fingers and the thumb, was evident. Weakness and occasional fasciculation of the flexor carpi ulnaris muscle could be elicited. There was claw deformity or fixed flexion of the fingers.

In the lower extremity, weakness of abduction-adduction of the toes was the earliest manifestation, to be followed by foot-drop and trophic lesions. Absorption of digits was commoner in the foot than in the hand.

The presence of contractures of the fingers appeared related to major or minor traumata and not merely to the paralysis.

Muscle biopsy could be obtained fairly consistently from near the motor point of the flexor carpi ulnaris muscle. Attempts at securing muscle tissue from near the motor point of the tibialis anterior muscle were unsuccessful.

Vital staining with methylene blue and the preparation of whole mounts appeared satisfactory for the study of intramuscular neural elements.

Normal muscle innervation comprised of interfascicular nerve, branches, subterminal fibres, motor end-plates, free nerve endings, and muscle spindles with sensory "end-organs" could be clearly discerned.

The normal motor end-plate appeared epilemmal, and consisted of a variable number of terminal filaments ending in endplate nuclei, presenting a fern-leaf pattern. One axon, one end-plate, one muscle fibre appeared to be the rule.

Pathological changes consisted of : (i) a reduction in the overall density or even loss of innervation of the affected muscle and (ii) histological alterations such as beading or fragmentation of the nerve fibres, shrinkage of the end-plates, and prominence of Schwann nuclei. Proliferation of endo and perineurium could be seen with sections.

Concurrent with these degenerative phenomena, regenerative change such as collateral branching and formation of growth cones and of immature end plates were witnessed, though very infrequently. Muscle regeneration was equally rare.

Various stages of muscular atrophy due to leprous neuritis were observed in H.-E. stained paraffin sections; these were compared to the changes reported in experimental and accidental nerve trauma and in muscular dystrophy.

The occurrence of a leprous myositis in some cases was indicated by the presence among the muscle fibres of inflammatory exudates consisting of mononuclear cells and occasional giant cells. This did not appear to contribute to the atrophy.

Rarely, in Fite stained sections, acid-fast organisms were detected in the intramuscular nerve twigs or connective tissue.

As a rule there was a fair degree of correlation between the clinical and the histological condition of the muscle, motor weakness varying directly with denervation and atrophy of the muscle. The intrafusal fibres were always spared.

While the status of intramuscular innervation in the moderately affected group of cases was comparable to that in the unaffected group the atrophy of muscle fibres was more pronounced in the former group. This suggested that histological changes in the muscle fibres precede those in the motor nerve fibres and endings. Similarly, degeneration of the motor end-plate appeared to antecede that of the sub-terminal nerve fibre.

This delay in the onset of neural changes, as also the long duration of the disease in most of the subjects, imply a rather slow progression of the neuritic process and provide adequate time for diagnosis and treatment.

As a routine diagnostic procedure for leprous neuritis an examination of simple haematoxylin-eosin stained muscle sections is recommended. The information provided by this could also help in selecting or assessing the result of a line of treatment, and in giving a prognosis.

Detailed examination of the swollen portion of an ulnar nerve obtained at autopsy has revealed a combination of ischaemic, inflammatory and destructive changes. Concurrent with the presence of acid-fast bacilli and a lepromatous exudate, the nerve trunk showed degeneration of the axis cylinders and myelin, and proliferation of the connective tissue and Schwann sheath elements. Besides the primary infective agent, the role of predisposing anatomical and mechanical factors in the causation of leprous neuritis is discussed. (Author's summary)

CURRENT TOPIC

EXPERIENCE IN THE MANAGEMENT OF PATIENTS MEDICALLY ADDICTED TO NARCOTICS

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While narcotic analgesics are of unquestioned value in the practice of medicine, the occurrence of narcotic addiction in the course of treatment for illness is acknowledgment of therapeutic failure. Indeed, prolonged, regular administration of narcotics by the physician to the point of addiction is a last resort in cases in which diagnostic procedures and specific methods of treatment have been exhausted, apparently without adequate effect, on a disease process associated with severe pain. The physician feels that to withhold narcotics from such patients would be unkind, sometimes humanely impossible. This is the basis for the belief, widely held by physicians and occasionally printed in textbooks,[1] that medically addicted patients should not be withdrawn from narcotics so long as the underlying illness has not been corrected. Furthermore, it is felt that the withdrawal process itself is a form of stress to which the sick person should not be subjected. It follows, then, that in the addicted patient suffering from a painful illness of chronic type the only therapeutic possibility is the life-long use of narcotics. However, because of the development of tolerance to the analgesic action of narcotics, eventually an impasse is reached in which the patient's daily narcotic requirements are high, yet the alleviation of pain is inadequate. In addition to being medically unsatisfactory, this situation is fraught with the possibility of economic and social disaster for the addicted patient and his family.

It is usually under such circumstances—at the end, it would seem, of their "therapeutic road", and often after some loss of both means and social status—that medically addicted patients are admitted to the U.S. Public Health Service Hospital, Lexington, Ky., one of the two federal hospitals dedicated primarily to the treatment of narcotic addiction. On the wards of the Lexington hospital it has been noted repeatedly and with some surprise not only that these patients, admitted for the treatment of addiction while still suffering demonstrably from the underlying illness, could be withdrawn safely from narcotics but that if they remained for the entire minimum period of treatment of narcotic addiction (135 days) they came to lead comfortable, often active lives while receiving merely the specific medicaments, nonnarcotic analgesics, or physiotherapy required by their underlying illness. To test these observations, the present study was carried out on a representative group of consecutively admitted male patients. As far as can be ascertained, no similar study has previously appeared in the literature.

[1] NIELSEN, J. M.: A Textbook of Clinical Neurology, ed. 3, New York, Paul B. Hoeber, Inc., 1951, p. 675.

DEFINITION OF MEDICAL ADDICTION

Kolb,[2] in 1925, in his classical study of personality types among narcotic addicts based on a group of 230 persons that was felt to be representative, at the time, of the addict population as a whole, found 9% to be "persons of normal nervous constitution to whom an opiate had been prescribed to the point of addiction to relieve the suffering of some prolonged physical condition." In applying Kolb's classification to the 1,036 patients admitted to the Lexington hospital during the fiscal year 1937, Pescor[3] found that 3·8% were normal persons who had become addicted to morphine "given legitimately for the alleviation of a painful or distressing disease." In 1944, Felix[4] reappraised the personality types among narcotic addicts and retained Kolb's category of "normal individuals accidentally addicted." Vogel, Isbell, and Champman[5] amplified the description of this group as being composed of normal persons who had received narcotics over an extended period of time in the course of an illness and who, following relief of their ailments, had continued to use narcotic drugs.

The figures in these reports have often been taken to represent the incidence of narcotic addiction during medical treatment. Used in that manner, these figures must be low, since addiction to narcotics in the course of illness is certainly not limited to persons of normal personality structure. For the purposes of this investigation, a medical addict is defined as one who states that he first received narcotics from a physician, to the point of addiction, in the course of treatment for illness. At the Lexington hospital, medical addicts fall into three sub-groups on the basis of the fate of their illness: 1. Narcotic addiction initiated during self-limited illness. Medical addicts in this group first received narcotics in the course of an illness from which they eventually recovered, such as lobar pneumonia or fracture of a long bone, but did not stop using narcotics. 2. Narcotic addiction associated with reversible illness. This group comprises medical addicts who, at the time of admission to the Lexington hospital were still suffering from the illness during which they had been addicted, and who recovered from this illness, such as renal calculi, through appropriate treatment during their period of hospitalization. Only a few such medical addicts are seen at the Lexington hospital. 3. Narcotic addiction associated with irreversible illness. In this group are medical addicts who first received narcotics in the course of an illness that is commonly painful, for which narcotics are thus likely to have been given, and in which improvement may occur through treatment, but in which the parthological process is essentially irreversi-

[2] KOLB, L.: Types and Characteristics of Drug Addicts, *Ment. Hyg.*, **9**: 300, 1925.

[3] PESCOR, M. J.: The Kolb Classification of Drug Addicts, Pub. Health Rep., supp. 1955, United States Public Health Service, Division of Sanitary Reports and Statistics, 1939.

[4] FELIX, R. H.: Appraisal of Personality Types of the Addict. *Am. J. Psychiat.*, **100**: 462, 1944.

[5] VOGEL, V. H., ISBELL, H. AND CHAPMAN, K. W.: Present Status of Narcotic Addiction, with Particular Reference to Medical Indications and Comparative Addiction Liability of Newer and Older Analgesic Drugs, *J.A.M.A.*, **138**: 1019 (Dec. 4), 1948.

ble, such as cardiovascular diseases, arthropathies, or causalgia. In these cases the clinical evidence was still present, so that the diagnosis could be established in the Lexington hospital.

Method

The method used in this survey grew out of the definitions just stated. Within one to two weeks after admission, all patients entering the Lexington hospital were interviewed by a member of the psychiatric social service section. Those male patients who answered affirmatively to ever having received narcotic drugs from a physician, either at the onset or at some time in the course of their addiction or during an illness, were further interviewed by the investigator. The investigator's interviews were conducted between the 90th and 110th hospital days and followed a standardized pattern. Data were first obtained regarding the patient's use of narcotics, a natural starting point for history-taking among addicted patients. This was followed by personal history data, past medical history, review of systems, history of illness during which the patient was addicted to narcotics, including treatment received prior to admission, status of that illness on admission to the Lexington hospital, and treatment received since admission. The patient was asked to evaluate his present state of health and physical comfort, his statement being recorded verbatim. As a means of verification, the interviewer then conservatively summarized in his own words what the patient had told him concerning the results of treatment. This rephrasing was adjusted if the patient did not acknowledge it as correct.

The patient's chart was then checked for supporting data in the initial history recorded by the admitting physician, in the physical examination, and in the laboratory reports. Opinions as to the patient's hospital course in the physicians', nurses', and psychiatric aides' notes were reviewed along with weight charts whenever available. Weight gain is a useful indicator in view of the loss of weight that usually accompanies prolonged addiction and because the addicted patient regards weight gain as a sign of returning health. Another criterion of recovery after withdrawal from narcotics is the subsidence of postwithdrawal insomnia. All patients admitted to the Lexington hospital are seen by a member of the psychiatric staff who, during his interview, obtains an independent addiction history. The record of this interview was consulted in each case to corroborate statements received from the patient in connection with the survey.

Any patient, tentatively diagnosed as a medical addict, in whose histories any significant contradiction was encountered was removed from the group of medical addicts. This occurred in seven cases. Also excluded were those medical addicts who did not remain for the entire minimum period of treatment of narcotic addiction.

Clinical Material and Results

Patients at the Lexington hospital fall into three legal categories: volunteers who may sign out any time; probationers from local courts, who would be taken to local jails for the remainder of their sentences if they left the hospital prior to the completion of their treatment for narcotic addiction; and federal prisoners, who may not leave until the expiration of their time.

During 1952, a total of 4,114 patients were admitted to the Lexington hospital. An arbitrary number of 1,500 consecutive admissions occuring between Aug. 8 and Dec. 9, 1952, were included in this study. They represented 36·4% of all admissions for that year. The composition of this sample with respect to sex and race is corpared with that of the whole group in Table 1.

Table 1—Comparison of Composition of All Admissions During 1952 with Sample of 1,500 Consecutive Admissions

	Race						Total by sex	
	White		Negro		Others			
	All	Sample	All	Sample	All	Sample	All	Sample
Males								
%	52	50·5	23·1	25	3·8	3·3	78·9	78·9
No.	2,139	758	950	375	157	50	3,246	1,183
Females								
%	...	...	...	...	...	...	21·1	21·1
No.	...	...	...	..	...	...	868	317
Total No. of patients				...		...	4,114	1,500

It is evident that the sample is representative of the total.

Because of differences in cultural and addiction patterns and in their treatment settings within the Lexington hospital, women, Orientals, informers, psychotics, and patients with a language barrier were excluded. This report, therefore, is based on 1,065 consecutively admitted male addicts, of whom 602 (56·5%) were volunteers, 282 (26·5%) probationers, and 181 (17%) federal prisoners. Admission of white patients numbered 694 (65·2%) and of Negroes, 371 (34·8%). Negro patients made up 32·1% of volunteers, 17·4% of probationers, and 71·3% of federal prisoners. Statistical characteristics of the male addict population are presented in Table 2. These data were obtained in each legal category by abstracting the chart of every fourth consecutive patient not classified as a medical addict.

Because of readmissions, the figure of 1,065 admissions represents 1,020 persons, 656 white and 364 Negro. Of this number, 182 left the hospital prior to being screened by the psychiatric social service, leaving 838 patients, 508 white and 330 Negro, whose statements regarding the manner of onset of addiction had been obtained. Among these patients, 277 (33·1%) had at some time received narcotics from a physician. Forty-seven of this number left the hospital prior to completion of treat-

TABLE 2—AVERAGE OF DATA BY RACE AND STATUS ON MALE NONMEDICAL ADDICTS

	Legal status						All nonmedical addicts	
	Volunteers		Probationers		Prisoners			
	White	Negro	White	Negro	White	Negro	White	Negro
Age on admission, yr.	40	25	41	26	36	26	39·7	25·7
Age at onset of addiction, yr. ...	29	20	26	22	24	21	27·2	20·9
Duration of addiction, yr.	11	5	15	4	12	5	12	4·5
No. of admissions ...	3·4	1·3	5·8	2·3	2·3	1·4	3·6	1·6

TABLE 3—DATA ON WHITE MALE MEDICAL ADDICTS

	Group 1		Group 2		Average of all medical addicts
	Average	Range	Average	Range	
Age on admission, yr.	49	31—69	45	23—59	47·4
Age at onset of addiction, yr. ...	31	18—54	38	20—66	32·9
Duration of addiction, yr.	18	1—35	10	0·5—33	14·8
No. of admission	5·5	1—20	3·6	1—12	4·9

ment. The remaining 230 patients were investigated according to procedure described. Among them 141 were recognised as medical addicts, 137 being white and 4 Negro, giving an incidence of 27% among white patients and 1·2% among Negro patients. If it were assumed that there were no medical addicts among the 182 who left the hospital prior to being screened, the respective incidences of medical addiction would be no less than 20·9% among whites and 1·1% among Negroes. However, a review at the rate of one in four of the charts of these 182 patients gave evidence that such an assumption was unnecessary.

The 141 medical addicts comprised 40 volunteers (28·4%), 90 probationers (65·8%), and 11 federal prisoners (7·8%). When compared with the composition of the male addict population, the medical addict group had half the incidence of volunteers and prisoners, twice the percentage of probationers, and one-twelfth the percentage of Negroes. On admission, medical addicts formed 6·6% of volunteers, 32% of probationers and 6% of federal prisoners. However, at the time of discharge medical addicts made up 31%, 36%, and 6% respectively, of the volunteers, probationers, and prisoners who had remained for the entire minimum period of treatment for narcotic addiction.

Among all male addicts, addiction to synthetic narcotics such as meperidine (Demerol) and methadone was entirely limited to patients receiving narcotics from physicians.

Statistical characteristics of medically addicted patients are given in Table 3. The probationers had 20% more previous admissions than the volunteers. Most probationers are former volunteer patients who, after signing out against medical advice during an earlier admission, re-enter the hospital for an entire period of treatment for drug addiction. A brief description of each of the three proups of medical addicts follows.

Group 1.—Marked addicts whose addiction had begun during self-limited illness numbered 89 (63·1%). They where white men except for one Negro. Their mean age of admission, 49 years, was higher than that of any other addict group. Even though they averaged four years older at the beginning of addiction than nonmedical addicts, they had the longest mean duration of addiction (18 years). In 25% of the group, narcotic addiction had begun during treatment for traumas of different severity. Another 30% had been chronic alcoholics. They had come to know the effects of morphine when it was given to them by a physician for alcoholic "shakes". Each patient averred that the conversion to opiates had been complete and well-nigh instantaneous; they had used no alcohol since. On admission, most of these patients showed only such deterioration of health as is incident to maintained addiction.[6] Their clinical management was identical with that of nonmedical narcotic addicts. However, in 21 of their number (23·6%) through advancing years, chronic painful illness had developed, for which they were continuing to receive opiates from a physician. Clinical investigation accord-

[6] ISBELL, H. AND WHITE, W. M.: Clinical Characteristics of Addiction, *Am. J. Med.*, **14**: 558, 1953.

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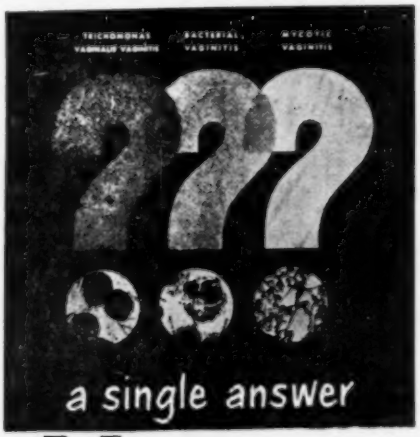

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ing to the method described confirmed that these patients fulfilled the criteria of medical addiction associated with irreversible illness (group 3). Despite their prolonged addiction history, the hospital course of these patients was identical with that of group 3 medical addicts, which will be specifically described below.

Group 2.—Medical addicts with reversible illness were represented by only two patients. Both were white and aged 25. One suffered from renal calculi and underwent uneventful lithotomy. There was no recurrence of symptoms during a year of observation in the Lexington hospital. The other patient had had recurrent left-sided migraine headaches for seven years. His treatment had included ergot preparations, psychotherapy, histamine desensitization, cobra venom, and different anodynes. Eventually he had become addicted to meperidine. At the Lexington hospital, earnest attempts to relieve pain by non-narcotic medical means were unsuccessful, with one exception. Procaine infiltration of the frontal branch of the left superficial temporal artery produced instantaneous, though temporary, relief of pain. This could not be duplicated by infiltration with isotonic sodium chloride solution. The frontal branch of the left superficial temporal artery was excised. The vessel was found to be normal on subsequent microscopic examination. Migraine headaches were relieved and did not return postoperatively during a period of three months.

Group 3.—Medical addicts with essentially irreversible illness form the most important group from the standpoint of this report. These patients numbered 50 (34·7%), 25 being admitted in each half of the 1,500 admissions. Their mean age on entry was 45 years, with a range of 23 to 59. Addiction had begun at 36, nearly a decade later than in the nonmedical addict. The mean duration of addiction had been 10 years, which was less than in the nonmedical addict. Three of the group were Negroes, in which medical addiction had begun earlier and had lasted longer.

One may therefore discern a "syndrome" of the chronically ill medical addict in which the typical patient is a man of middle age, with late onset of addiction (fourth decade), demonstrably ill, and addicted to morphine or to a synthetic narcotic drug. Among these patients, a diagnosis of cardiovascular disease was established in nine. Thirteen had gastrointestinal disease, 5 pulmonary disease, 11 bone or joint disease, and 12 neurological illnesses. Withdrawal from narcotics was accomplished gradually by the methadone substitution method.[7] The period of the withdrawal was determined individually for each patient, depending on his physical condition and on the dosage during addiction. In this series, the duration of withdrawal ranged from 1 to 15 days. The medical and addiction histories, diagnoses, diagnostic evidence, and treatment are summarized in Table 4. Due to limitation of space, only 40 representative cases are listed. In that table the results of 90 to 110 days of treatment are presented in terms of the management of clinical exacerbations, work assignment carried out in the hospital, ability to sleep spontaneously, and weight gain (whenever available). The patient's own statement is quoted in the last columns of the table. It is followed by a letter symbol in brackets that summarizes the combined opinions of patients and staff as to the patient's general condition after 90 to 110 days of hospital treatment. (A) stands for a very good result, (B) for a good one, (C) for a fair one, and (D) for no improvement. On the basis of such coding, the following numerical summary is possible: (A) was applied in 22 cases, (B) in 20, (C) in 7, and (D) in 1.

Results in Group 3.—Of 50 patients of diverse personality structure, admitted for the treatment of narcotic addiction while still suffering from a persistent and painful illness during which they had been addicted, all were withdrawn safely from narcotics and 42 (84%) stated that they felt well or very well while receiving merely the specific medicaments, non-narcotic analgesics, and physiotherapy required by their underlying illness. Many were able to hold a work assignment in the hospital. A similar result was observed among the 21 older medical addicts in group 1 who were mentioned earlier as also fulfilling the criteria for group 3.

COMMENT

Environment: The setting in which these results were obtained is relevant. The Lexington hospital is a closed institution in which access to contraband narcotics is prevented. It is staffed by physicians, other hospital personnel, and work supervisors who combine in the care of the addicted patient during an initial and brief clinical period of withdrawal from narcotics which is followed by a longer rehabilitative period. Daily life in the Lexington hospital may be compared with that of a partially self-sufficient community in which each member is assigned work according to his abilities. Bed, board, recreation facilities, and some entertainment are provided, and regular hours are kept. The medical, surgical, and diagnostic facilities of a general hospital are available, including physiotherapy. It is understood that narcotics are not prescribed in the absence of definite medical or surgical indications. However, when these exist (as in acute myocardial infarction or massive pulmonary hemorrhage or preoperatively), narcotics are administered in conformity with established medical practice in cases of similar nature. The staff adheres to a stated policy in determining the time of discharge for each patient. During this survey, the minimum period of treatment was 135 days. This was extended, when required, to provide at least 100 days of treatment from the last dose of narcotics. It may be seen that the Lexington setting incorporates a number of features that the individual physician could reproduce for the medically addicted patient in an attempt to obviate the continued need for narcotics. Perhaps most important is the knowledge that withdrawal from narcotics may be accomplished safely during treated chronic illness.

Medical addiction.—In the definition of medical addiction used in this study, reliance is placed on the patient's statement that he first received narcotic from

[7] WIKLER, A.: Drug Addiction, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1953, Vol. 8, p. 17. Isbell, H. and others: Liability of Addiction to 6-Dimethylamino-4-4-diphenyl-3-haptanone (Methadon, "Amidone" or "10820") in Man, *Arch. Int. Med.*, **82**: 362 (Oct.), 1948.

TABLE 4.—*Case Histories of Medical Addicts with Essentially Irreversible Painful Illness (Group 3)*

Case	Age, Yr.	Race	Medical Addiction History: Illness During Which Addicted	Medical Addiction History: Treatment Prior to Admission	Medical Addiction History: Yrs. of Illness	Medical Addiction History: Yrs. of Addiction	Abstract of Hospital Record: Diagnosis	Abstract of Hospital Record: Diagnostic Evidence	Abstract of Hospital Record: Treatment	Abstract of Hospital Record: Days of Withdrawal	Objective Results: Management of Exacerbations	Objective Results: Work Assignment Held	Objective Results: Weight Gain Lb.	Subjective Results: "How Do You Sleep?"	Subjective Results: "How Do You Feel Now?"
Patients with Cardiovascular Disease															
1	54	W	Heart disease	Low salt diet, digitalis, diuretics, aminophylline, dihydromorphinone	12	11	Rheumatic mitral valve deformity, class 3C to 2B*	Mitral presystolic and systolic murmur, enlarged heart, congestive failure: EKG: chronic auricular fibrillation	Digitalis, diuretics, low salt diet	15	Same regimen adjusted	Limited duty	...	Well	Pretty good (B)†
2	52	W	Asthma; heart disease	Epinephrine, ephedrine, ammmoium chloride, activity not restricted, morphine	15	15	Bronchial asthma; arteriosclerotic heart disease, class 3C*	Anasarca, dyspnea on least exertion, enlarged heart, cyanosis, basal rales; EKG: left bundle branch block	Bed rest, low salt diet, mercurials, rectal aminophylline	13	Aminophylline intravenously, phenobarbital	None	...	Fair	Pretty well (B)
3	54	W	Gall-bladder disease	Diets, antacids, antispasmodics, sedation, cholecystectomy, meperidine codeine	22	12	Autonomic imbalance; biliary dyskinesia	BP 110/70 to 200/120 mm. Hg.; epigastric pain, vomiting	Phenobarbital, atropine, intravenous fluids, Sippy diet.	1	Same regimen adjusted	Limited duty	8	Moderately well	Pelling well (B)
4	35	W	Rheumatic heart disease; high BP	Digitalis, glyceryl trinitrate, diuretics, total sympathectomy, morphine	18	7	Rheumatic aortic and mitral valve deformity; angina; class 3C to 2B*	Double murmurs at base and apex, enlarged heart, congestive failure; roentgenogram: bilateral cardiac enlargement	Bed rest, low salt diet, diuretics, vasodilators	10	Vasodilators	Farm	...	Well	Good (A)
5	50	W	Myocardial infarcts	Bed, oxygen, meperidine, glyceryl trinitrate, cervical sympathectomy, medical thyroidectomy (radioactive iodine)	5	5	Arteriosclerotic heart disease; angina*	EKG: healed posterior wall infarct; BMR:—21%	Bed rest, vasodilators, digitalis, thyroid extract 32 mg. daily	10	Self-imposed limitation of activity	None	...	Well	Very little chest pain; feel quite good (A)
6	59	W	Angina	Digitalis, diuretics, low salt, dihydromorphinone	13	13	Arteriosclerotic heart disease; Class 3D to B*	Ascites, leg edema, dyspnea	Low salt diet, mercurials, digitalis, restricted physical activity	14	Same regimen adjusted	None	...	Well	Comfortable (B)

7	47	W	Rheumatic heart disease	Digitalis, diuretics, morphine	13	13	Rheumatic aortic and mitral valve deformity; class 3C*	Dyspnea at rest, cyanosis, aortic systolic and double mitral murmurs, peripheral edema, right pleural effusion	Low salt diet, digitalis, mercurials, restricted physical activity	10	Same regimen adjusted	None	0	All right	As well as can be expected with that ticker of mine (B)
8	41	W	High BP; stroke; headache	Hospitalised for stroke; then, demanding work and meperidine	2	0·5	Hypertensive vascular disease; chronic brain syndrome	BP 180/120 to 210/125 mm. Hg.; spastic right hemiparesis; EKG: left axis deviation	Phenobarbital, restricted physical activity	12	Same regimen adjusted, salicylates	None	10	Right well	Well, except for headaches (B)
							Patients with Gastrointestinal Disease									
1	51	W	Gallbladder disease	Diets, belladonna, antacids, dihydromorphinone, morphine	17	3	Psychophysiological gastrointestinal reaction	Fat intolerance; right upper quadrant tenderness; GI and gallbladder roentgenograms normal	Bland diet, belladonna, antacids, and phenobarbital initially; later, full diet	2	Belladonna, antacids	Farm	10	Well	Feel good (B)
3	54	W	Gallbladder disease	Diets, bile salts, antacids, morphine	10	3	Chronic cholecystitis	Tender right upper quadrant; roentgenogram: nonfunctioning gall-bladder	Bile salts, belladonna, antacids, bland diet	5	None	Shoe repair	20	Fine	Very well (A)
4	35	N	Stomach ulcers	Milk, antacids, belladonna, morphine	13	13	Duodenal ulcer and hemorrhage	Roentgenogram: deformed duodenal cap	Sippy diet, phenobarbital initially	5	None	Orderly	...	Good	Good (B)
5	33	N	Stomach ulcers	Hospitalization, diets, belladonna, antacids, morphine (later heroin illegally)	6	0·5	Duodenal ulcer	Roentgenogram: deformed duodenal cap	Progressive, then advanced Sippy diet, belladonna, antacids	5	Same regimen adjusted	None	20	Well	Well (B)
6	48	W	Stomach ulcers	Diets, antacids, antispasmodics, morphine, meperidine, subtotal gastrectomy	10	6	Subtotal gastrectomy	Epigastric tenderness; roentgenogram: subtotal gastric resection	Bland diet	7	None	Orderly	18	Well	Fine (A)
7	29	W	Stomach ulcer	Hospitalization, diets, antacids, antispasmodics, morphine	8	1	Duodenal ulcer	Epigastric tenderness; roentgenogram: apex of duodenal bulb narrowed	Advanced Sippy diet, antacids, methantheline	4	Phenobarbital for short periods	Handyman	11	Well	Well (B)
9	40	W	Stomach disease	Diets, cholecystectomy, antacids, antispasmodics, morphine (heroin illegally)	6	5	Duodenal ulcer	Roentgenogram: deformed duodenal bulb	Belladonna, antacids, bland diet; then bland diet alone	11	None	Limited duty	14	OK	Well (B)
10	43	W	Stomach ulcer	Diets, belladonna, antacids, concentrated opium, subtotal gastric resection	10	7	Subtotal gastrectomy	Vomiting; epigastric tenderness: roentgenogram: subtotal gastric resection	Advanced Sippy diet, antacids, methantheline	5	None	Clothing room	0	Well	Feel like myself now (A)
12	58	W	Stomach ulcer	Antacids, belladonna, gastric operation, irregularly observed diets, morphine	20	5	Subtotal gastrectomy; marginal ulcer	Diagnosed by barium roentgenogram study	Advanced Sippy diet, methantheline	4	None	Limited duty	...	Very well	Very well (A)

TABLE 4—*Contd.*

Case	Age, Yr.	Race	Medical Addiction History: Illness During Which Addicted	Medical Addiction History: Treatment Prior to Admission	Medical Addiction History: Yrs. of Illness	Medical Addiction History: Yrs. of Addiction	Abstract of Hospital Record: Diagnosis	Abstract of Hospital Record: Diagnostic Evidence	Abstract of Hospital Record: Treatment	Abstract of Hospital Record: Days of Withdrawal	Objective Results: Management of Exacerbations	Objective Results: Work Assignment Held	Objective Results: Weight Gain Lb.	Subjective Results: "How Do You Sleep?"	Subjective Results: "How Do You Feel Now?"
Patients with Pulmonary Disease															
1	36	W	Asthma	"All medicines tried", skin tests, morphine	27	8	Bronchial asthma	Dyspnea, sputum, musical rales	Aminophylline intravenously at first; ephedrine, epinephrine	2	Aminophylline orally	Elevator	25	Very well	Very well (A)
2	58	W	Pulmonary tuberculosis	Sanatoria, morphine	33	33	Pulmonary tuberculosis inactive; bronchiectasis	Dyspnea, 3-layer sputum; roentgenogram: fibrosis both apices	Bed rest	10	Ephedrine	Limited duty	...	Poor	Fairly well (C)
3	34	W	Tuberculosis of lungs and spine	Sanatoria; then bed rest and morphine at home	10	9	Pulmonary tuberculosis, moderately advanced, active; tuberculosis of spine, inactive	Roentgenogram; fibrocalcific infiltrations both upper lungs, fusion D4-D5; sputum positive	Bed rest, streptomycin, p-aminosalicylic acid	12	Salicylates	None	15	Well	Well (B)
4	64	W	Asthma	"Nothing helps except morphine"	30	25	Bronchial Asthma	Musical rales and prolonged expiration	Aminophylline-ephedrine-phenobarbital tablets	2	Aminophylline intravenously	Limited duty	21	Well	Fine (A)
Patients with Bone and Joint Disease															
1	50	W	Tuberculosis of spine	Sanatoria, 3 spinal fusions dihydromorphinone	24	24	Tuberculosis of thoracic spine, inactive	Roentgenogram: stable tuberculosis and surgical fusion of lower dorsal vertebrae	Physiotherapy, salicylates	...	Bed board, salicylates	Library clerk	5	Fair	Fairly well (C)
2	49	W	Osteomyelitis, left hip	Bed, casts, curettages, morphine, methadone	38	26	Chronic osteomyelitis, inactive, with pain	Wide scars, left thigh; roentgenogram: mark-to arthritis and bony ankylosis of left hip joint	Physiotherapy, salicylates	8	None	None	...	Fine	Excellent condition (A)
3	47	W	Osteomyelitis after fracture	Frequently hospitalised for recurrences; morphine	13	13	Osteomyelitis and old fracture of right tibia and fibula	Draining sinus; roentgenogram: osteomyelitis, sequestrum, old fracture	Penicillin	4	None	Kitchen	...	All right	Good (B)
5	38	W	Painful right hip	Surgical "cuping" right hip, morphine	3	1	Prosthetic head, right femur	Limited motion right hip; roentgenogram confirms	Physiotherapy, salicylates, limited activity	5	Same regimen adjusted	None	...	Well	Considerably improved (A)

6	44	W	Arthritis	Salicylates, physiotherapy, morphine	25	13	Rheumatoid arthritis of spine	Kyphosis; roentgenogram: Marie-Strumpell arthritis of spine	Sought no treatment	6	None	Clerk	...	Well	Very well (A)
7	59	W	Arthritis of spine	Salicylates, physiotherapy, x-ray therapy, cortisone, codeine, meperidine	20	2	Rheumatoid arthritis of spine	"Poker" spine; roentgenogram: extensive Marie-Strumpell arthritis of spine	Salicylates	9	Cortisone codeine	Limited duty	...	Well	Excellent (A)
8	45	W	Osteomyelitis in stump of left leg	Revision of stump, excision of neuromas, dihydromorphinone	12	12	Left midcalf amputation	Well-healed stump, painful on manipulation	Sought no treatment	7	None	Clothing room	...	On and off	Fair (C)
9	46	N	Arthritis	Long hospitalization at 17, morphine	33	28	Rheumatoid arthritis, multiple	Swelling and limitation of motion in hands and feet	Salicylates, physiotherapy	9	Same regimen adjusted	Farm	...	OK	Good (B)
11	55	W	Arthritis of neck	Salicylates, morphine, physiotherapy for limited neck motion	5	5	Cervical osteoarthritis, C5-6-7	Atrophy of shoulder and arm muscles; spastic paraparesis; roentgenogram: disc degeneration and extensive arthritic changes	Tests only, explanation of diagnosis	6	Salicylates	Limited duty	...	Fair	Fair (C)
							Patients with Neurological Disease								
1	57	W	Diabetic leg pain	Protamine zinc insulin, full diet, vitamins, dihydromorphinone	4	3	Diabetic neuropathy	Diabetic retinitis; peripheral neuritis; roentgenogram: demineralization of distal leg bones	Insulin mixture, diabetic diet, vitamin B_1 and B_{12}	9	Salicylates	None	...	Well	Fairly well (B)
2	40	W	Migraine	Histamine, electroshock, diuretics, psychotherapy, dihydromorphinone, methadone	23	10	None	None; "Few headaches while here"	Sought no treatment	2	None	Orderly	12	Never well	Feel pretty well (B)
3	48	W	Back injury	Morphine, laminectomy, fusion cast	1	1	Spondylolisthesis, L5-S1; surgical fusion L4-L5-S1	Roentgenogram confirms; tenderness	Limited duty, physiotherapy, salicylates	7	Mephenesin, quinine	Carpenter	15	Well	Much better than on drugs (A)
4	51	W	Sciatica of left leg	Bed rest, then up on crutches, codeine, morphine	13	13	Herniated intervertebral disc L5-S1	Diminished left knee and ankle reflexes; hypesthesia; roentgenogram: narrowed L5-S1 interspace	Physiotherapy, salicylates	4	Same regimen adjusted	Kitchen	...	Well	Very well (A)
5	34	W	Cord Tumor	Laminectomy, postoperative diagnosis, scar tissue only; morphine	4	4	Psychophysiological musculoskeletal reaction	Able to walk on crutches only; neurological examination normal	Encouragement, limitation of secondary gain, two canes; then one cane	12	Physiotherapy	None	...	Well	Fair (A)

TABLE 4—*Contd.*

Case	Age, Yr.	Race	Medical Addiction History: Illness During Which Addicted	Medical Addiction History: Treatment Prior to Admission	Medical Addiction History: Yrs. of Illness	Medical Addiction History: Yrs. of Addiction	Abstract of Hospital Record: Diagnosis	Abstract of Hospital Record: Diagnostic Evidence	Abstract of Hospital Record: Treatment	Abstract of Hospital Record: Days of Withdrawal	Objective Results: Management of Exacerbations	Objective Results: Work Assignment Held	Objective Results: Weight Gain Lb.	Subjective Results: "How Do You Sleep?"	Subjective Results: "How Do You Feel Now?"
7	23	W	Broken back and paraplegia	Immobilization, laminectomy, cordotomies, morphine meperidine	2	2	Compression fracture L-1; flaccid paraplegia	Paralysis and wasting, both legs; atonic cord bladder; roentgenograms confirm	None	4	None	None	...	Well	Very well (A)
9	41	W	Right facial pain	Salicylates, histamine, supraorbital neurectomy, sphenopalatine blocks, morphine	13	13	Right "sphenopalatine neuralgia"	Vasodilatation and lacrimation in right eye when in pain	Lidocaine block of right sphenopalatine ganglion; infusions of calcium, ergotamine tartrate, and procaine	5	Barbiturates occasionally	Handyman	...	Fair	Have not felt so well in 13 years (A)
10	51	W	Tabes dorsalis with gastric crises	Antileutic therapy, symptomatic therapy, morphine; well between attacks	20	5	Tabes dorsalis with gastric crises	Argyll-Robertson pupils, absent knee and ankle reflexes, attacks of abdominal pain, nausea and vomiting	Intravenous fluids, phenobarbital, intercostal nerve blocks	9	Narcotics intermittently	None	20	Fair	Well between attacks (D)
11	37	W	Causalgia of right foot	Fractured by land mine in World War II; operation, morphine	9	5	Neuropathy right tibial nerve due to trauma; causalgia	Dysesthesia in distribution of right tibial nerve; roentgenogram: healed fracture right tibia and fibula and demineralization of right lower leg bone	Sought no treatment	4	No treatment sought	Clothing room	...	Fine	Very well. Can handle that pain by myself now (A)
12	27	W	Painful phantom arm; heart disease	Right arm blown off in World War II; long hospitalization, morphine, quinidine	7	7	Painful phantom right arm; anxiety reaction	Tachycardias, sweating, tremors, clammy hands	Sedation	0	Psychiatric care	Orderly	12	Well	Much better (A)

* Nomenclature and Criteria for Diagnosis of Diseases of the Heart, ed. 4, New York, New York Heart Association, 1939.
† Code letters represent clinical evaluation of result, as described in text.

a physician. For verification, the patient's recorded statement on that point during this and previous admissions were reviewed. Veracity therefore was equated with consistency. Because of the nature of drug addiction, useful information from external sources was not obtainable. Similarly, when any physician is called on to attend an addicted patient, the patient's statement as to how he became addicted is all that is usually available to the physician.

There is good reason to believe that among persons who become addicted to narcotics during treatment for illness a number would accept withdrawal from narcotics in much the same cooperative spirit with which treatment of postoperative phlebitis or other complications would be accepted by a patient recovering from an abdominal operation. The factors of association with other addicts and of access to illegitimate sources of supply are absent. The person remains motivated by the social condemnation of opiate addiction. On his part, the physician has the same continuing responsibility to his patient for the treatment of medical narcotic addiction that he would assume in cases of other therapeutic complication. To dismiss a patient from one's care soon after realizing that he is addicted is both physiologically and psychologically unjustifiable and socially unsound. Planned withdrawal from narcotics should be attempted after informing the patient that it is an uncomfortable, but relatively brief and definitely self-limited, period. If withdrawal fails because of marked manipulative behaviour directed at securing narcotics, arrangements should be made for direct admission to an institution for the treatment of opiate addiction. It is generally agreed that institutional treatment is required for the confirmed addict. An excellent review of the management of such addicts has recently appeared in the Journal.[8]

Methods of withdrawal.—It has been stated in this report that, despite the presence of essentially irreversible illness, withdrawal from narcotics may be accomplished safely if it is done gradually. The methadone substitution method[7] is used routinely at the Lexington hospital. As an alternative plan, gradual withdrawal of the drug of addiction may be carried out. However, the methadone substitution method is recommended in cases of meperidine addiction. The length of action of meperidine being relatively short, injections would be required at intervals of two to three hours, both day and night, to prevent the appearance of abstinence changes between doses. Whatever the method of withdrawal, a procedure that does not use opiates may result in a death in sick persons addicted to large doses of narcotics.

Special care has to be exercised in patients with cardiac insufficiency. Patients with active tuberculosis may be withdrawn gradually from narcotics without danger of aggravating the tuberculosis process. All addicted patients admitted to the tuberculosis ward of the Lexington hospital are withdrawn from opiates unless the disease is so advanced that death is likely. After withdrawal, they gain weight, observe bed rest, and sleep spontaneously. Cough, if distressing, is treated with minimal amounts of codeine, although other medicaments to relieve cough usually suffice.

This report does not refer to cases of painful, fatal illness. For patients such as those dying of carcinoma, the question of withdrawal does not arise. The concern of the physician is primarily with relief of suffering and not with restoration to useful life.

Management of chronic pain.—In this study it has been demonstrated that, under the conditions described, after withdrawal it is possible for former opiate addicts to adjust without narcotics to chronic pain or discomfort incident to chronic illness. It should be noted that the term "medical addict" as defined in this report implies nothing with regard to the patient's preaddiction personality. Even if clear criteria were available for the diagnosis of normal persons (in the psychiatric sense), it is hardly likely that all or most of the patients included in this study would fall into that category. It seems, therefore, that, even when the problem is complicated by chronic, painful disease, successful withdrawal and satisfactory adaptation without narcotics are dependent on factors other than the preaddiction personality. At least in the setting described in this report, the attitudes and other activities of the physician appear to play a decisive role in many cases.

Morphine is not the answer to chronic pain. Because of the development of tolerance to the analgesic effects of morphine, alleviation of pain becomes inadequate. Under such circumstances, the physician, by gradually withdrawing narcotics, does not deprive the patient of any actual benefit but protects him and his family from the possible legal, social, or economic difficulties attendant on opiate addiction. The administration of morphine to a patient with chronic pain is a short-lived type of kindness. Long-term kindness would begin when opiates are withheld or withdrawn in favor of other therapeutic measures.

Clinically, the distinction of organic pain from psychogenic pain cannot be sustained and should be discarded. No matter how tangible its source of origin, in the final analysis pain is a psychic phenomenon. It is invariably both a sensory and an emotional experience. Factors affecting any aspect of this whole will modify the total experience. In meeting the challenge of chronic pain, management directed simultaneously toward several aspects of the total experience is most likely to be successful. Means of relieving chronic pain other than prescription of opiates should be exhausted one by one. Such measures include the use of non-narcotic medicaments, consultations with specialists, physiotherapy, radiation therapy, anesthetic blocks, and surgical procedures for the relief of pain. At the same time, adjustments in the patient's life setting should be an intrinsic part of therapeutic pain: increase or, more commonly, decrease of physical activity; rest periods, possibly combined with self-administered physiotherapy; simplifications or increase of responsibilities, at work or at home. These are but a few examples.

[8] What to Do with a Drug Addict, report of the Council on Pharmacy and Chemistry, *J.A.M.A.*, **149**: 1220 (July 28), 1952.

Role of physician.—A major factor in this adjustment is the performance of the physician. The physician who views pain traditionally, as merely a symptom of physical disease, fails to see that he has before him a personality experiencing pain within an individual mental framework. He disregards the emotional changes that arise with pain (such as increased dependency needs and self-centeredness) and consequently fails to utilize the resources of that personality in adapting to pain. Such a physician finds it necessary to administer narcotics frequently and, because he offers nothing else, tends to make the use of narcotics essential to his patients. On the other hand, the attentive physician who is able to offer his patients sympathetic understanding, steady support, and realistic perspective obtains similar results while resorting infrequently to habit-forming drugs. He prescribes drugs as a specific part of the relationship between physician and patient and not as a substitute for that relationship.

Finally, the physician has a continuing responsibility in the prevention of medical addiction by consistently limiting the administration of narcotics to patients presenting definite indications. There is increasing evidence that a basic reorientation is needed in situations in which the routine use of opiates had appeared well established. To cite only one example, Papper and associates[9] have shown that over one-third of unselected patients on an active surgical service had no significant postoperative pain. In determining indications, it is important to evaluate patients individually. Special care should be exercised in prescribing narcotics for those who are or have been alcoholics and for patients whose complaints are markedly out of proportion to the physical findings. Narcotics are not the proper means of alleviating distress resulting from emotional conflict.

SUMMARY

In a representative group of 1,020 male opiate addicts consecutively admitted to the Public Health Service Hospital, Lexington Ky., the incidence of patients medically addicted to narcotics was 27% among whites and 1·2% among Negroes. The former percentage is considerably higher than has previously been recognized. Among medical addicts, those patients who had been addicted during self-limited illness were essentially healthy on admission to the Lexington hospital. Their management was identical with that of nonmedical addicts. A "syndrome" of the chronically ill medical addict is identified: the typical patient is a man of middle age with late onset of addiction (fourth decade), demonstrably ill, and addicted to morphine or to a synthetic narcotic that he first received from a physician, to the point of addiction, during treatment for illness. Among 50 such medical addicts studies, all had been admitted for the treatment of narcotic addiction while suffering from an essentially irreversible painful illness, during treatment of which they had become addicted. All were withdrawn safely from narcotics by the methadone substitution method. After these patients had been abstinent from narcotics for about 100 days, 84% stated that they felt well or very well while receiving merely the specific medicaments, non-narcotic analgesics, and physiotherapy required by their underlying illness. Many were able to hold a work assignment in the hospital.

Chronic illness need not be regarded as an indication for the continued administration of narcotic drugs. The successful management of chronic pain without the prescription of narcotics rests on the recognition that pain is never solely a symptom of physical diseases but is an experience of the total personality. Treatment, therefore, must be directed simultaneously towards several aspects of the total experience.

—Reproduced by permission from the *Journal of the American Medical Association*, **156**: 684 (Oct. 16), 1954.

[9] PAPPER, E. M., BRODIE, B. B. AND ROVENSTINE, E. A.: Postoperative Pain; Its use in the Comparative Evaluation of Analgesics, *Surgery*, **32**: 107, 1952.

NOTES AND NEWS

I.M.A. Research Fellowships

The Indian Medical Association has provision for four Research Fellowships of the value of Rs. 250/- each per month for one year in the first instance. Two of these fellowships are awarded by the I.M.A. and the other two by Messrs. Unichem Laboratories of Bombay under the auspices of the I.M.A. Of the latter two fellowships, one will be awarded for work on some pharmacological subject.

Applicants must be members of the I.M.A. and conform to the regulations for award of these fellowships, copies of which may be obtained on request from the Indian Medical Association (Central Office), Hanging Bridge, Daryaganj, Delhi 7.

The applications should reach the Central Office, I.M.A. not later than 30th September, 1956.

Microfilm and Photocopy Service

The Indian Council of Medical Research established in 1948 two Microfilm and Photocopy Service Units, one at the Central Research Institute, Kasauli, and the other at the Tata Memorial Hospital, Bombay. These Units have been set up with the object of supplying to medical and other scientific institutions, teachers, research workers and individuals, copies of articles from journals, foreign or Indian, which are not readily available.

The aim of this service is to make available to scientific workers important research articles at cost price. The rates are

Microfilms: Rs. 3/- for the first ten pages of a reference or a portion thereof and Rs. 1/8- for the subsequent ten pages of reference or part of it.

Photocopy: Size of paper—Upto 6″×11″ @ As. -/8/-; upto 11″×17″ @ As. -/12/-; upto 17″×23″ @ Rs 1/4/—per page per copy.

Workers who desire to have microfilm or photocopy of any article are requested to communicate complete reference to the Officer-in-Charge of the Unit and the source, if known, of the Journal where it is available. The Unit will undertake to procure the journal and supply copies of articles in the minimum time possible.

Postgraduate Training in Public Health

A WHO Conference of Postgraduate Training in Hygiene, Preventive Medicine and Social Medicine opened in Zagreb, Yugoslavia, on 2 July 1956. The participants were prominent administrators and educators in public health from 19 countries in Europe. The Conference was arranged by the Yugoslav Government and the WHO Regional Office for Europe.

The Zagreb Conference follows two related meetings arranged in Europe by the World Health Organisation. The first was held at Nancy, France, in 1952, and was concerned with undergraduate teaching. The second was held at Goteborg, Sweden, in 1953, and was concerned with postgraduate training. The questions that were discussed at the present conference included the following.

(a) What are the needs for various categories of health officers in different countries? (b) What training is needed for these categories? (c) How can training institutions best be organised to meet these needs? (d) What methods can be developed for closer co-operation between schools and training centres of public health in Europe?

The aims of the Conference were to analyse present developments in Europe, to define desirable future policies and trends, and to make proposals on how the World Health Organisation might best develop its work of assisting governments in the field of postgraduate public-health training.

Malaria Strategy Set by WHO Expert Committee

A strategy for total war against malaria, with the aim of eradicating the disease throughout the world, has been drawn up by the WHO Expert Committee on Malaria. The group, which held its 6th session in Athens, under the chairmanship of Professor G. Livadas, of Athens, not only confirmed that malaria eradication was feasible, but that its enormous economic and social advantages made it the only rational policy to adopt.

The sums required to achieve eradication within a definite time, although substantial, are much less than the cost of continued malaria control of a less intensive character on a long-term basis. Moreover, at the present time, several international and national agencies, such as UNICEF, UN Technical Assistance and the US International Cooperation Administration are ready to assist governments that embark on such a programme.

The members of the Committee, pooling experience gained in such widely separated areas as Taiwan and Italy, India and Venezuela, recognised that one of the most urgent reasons for carrying out malaria eradication with the least possible delay, was the growing resistance of the mosquito carriers of malaria to insecticides like DDT.

The report underlined the need for careful study of each country or area where malaria is a problem before applying the strategy. Recommendations were made concerning the use of preventive and therapeutic drugs and additional help to spraying operations. The Committee's report also took note of some of the gaps in knowledge that must be filled before all problems can be solved. The danger of malaria crossing frontiers and re-infecting cleared areas was given serious attention and WHO was asked to help countries take the necessary steps to coordinate their efforts and protect each other.

Malaria on a global scale reached its peak in the last century but, despite its noticeable decline, there are still thought to be more than 250 million people in the world who suffer attacks each year, while about 2¼ million die of the disease or its consequences.

Health Education Conference

India will play host to a session of the South-East Asia Regional Committee of the World Health Organisation in the last week of September. The session will be held at Patiala House in New Delhi. The main subject to be discussed by the regional committee will be health education. Afghanistan, Burma, Indonesia, Nepal, Ceylon and Thailand will attend the conference besides India. An exhibition on health education depicting progress made under the second Five-Year Plan will be organised by the Union Health Ministry.

Medical Relief in Rural Poona

The extension of medical relief to rural Poona was announced on 20-8-56 before a meeting of the Health Sub-Committee of the District Development Board.

With twenty-nine new primary health centres sanctioned by the Government and expected to start functioning shortly, Poona District will have 67 such centres serving the rural population. Each unit staffed by one doctor, one nurse, one midwife and a sanitary inspector will afford relief to villages within a radius of seven miles throughout the district, except Mawal area. Even so there will be only one health unit for a population of 15,000.

American College of Chest Physicians Prize Essay Contest

The Council on Undergraduate Medical Education of the American College of Chest Physicians offers three cash awards to be given annually for the best contributions prepared by undergraduate medical students on any phase in the diagnosis and treatment of chest diseases (heart and/or lungs).

Upon the recommendation of the Council, which was approved by the Board of Regents of the College at their recent annual meeting, the awards will be increased for the 1957 contest. The first prize will be $500; second prize will be $300; and third prize $200. Each winner will also receive a certificate of merit.

The winning contributions will be selected by a committee of chest specialists and will be announced at the 23rd Annual Meeting of the American College of Chest Physicians to be held in New York City, May 29 - June 2,

1957. All manuscripts become the property of the American College of Chest Physicians.

College of Physicians of Philadelphia

On July 14, 1956, the College of Physicians of Philadelphia awarded the Alvarenga Prize for 1956 to George N. Papanicoloau, M.D., Director of the Papanicoloau Research Laboratory of Cornell University Medical College, for his outstanding work in the early detection of cancer.

The Alvarenga Prize was established by the Will of Pedro Francisco DaCosta Alvarenga of Lisbon, Portugal, an Associate Fellow of the College of Physicians of Philadelphia, to be awarded annually by the College of Physicians on the anniversary of the death of the Testator, July 14, 1883

Two-year Drive Against T.B. in Scotland

Scottish health authorities are worried at the large number of tuberculosis cases being reported. To attack the "reservoir of infection" they are therefore planning a national case-finding drive against the pulmonary form of the disease. It promises to be more ambitious than anything of the sort previously attempted in Great Britain. The Ministry of Health and the RAF are leading diagnostic units for the two-year campaign.

World Found to Have 1,200,000 Doctors

The world now has 1,200,000 physicians, and the 595 medical schools of 85 countries turn out between 50,000 and 60,000 new doctors every year, according to a recent study by the World Health Organization, prepared by Dr. James L. Troupin, chief of WHO's Section of Assistance to Educational Institutions.

The doctors, however, are distributed very unevenly among the world's 2,500 million people. Fourteen countries are fortunate enough to have one doctor to serve up to every 1,000 people, as compared with 222 others where there is only one doctor for every 30,000 inhabitants or more.

Nine countries, it also shows, have one medical school each for less than one million people each. Thirteen, on the other hand, have only one school each for between 9 million and 17 million people. There is thus a definite need for building medical schools in these lands, as in other countries.

Advanced Nursing Education in Europe

The WHO Conference on Post-Basic Nursing Education was held at Peebles, Scotland, some time ago. In the course of a 14 day meeting, existing facilities for advanced nurse training in Europe were reviewed and future developments considered.

The following gives some of the points that arose out of the discussions and are to be dealt with in the final report of the Conference.

The all-important objective of advance in nursing education is the improvement of nursing practice resulting in benefit to the community. In the past, courses have been limited in many ways and should today be complemented by teaching in public health, particularly in health education and the psychology of teamwork relations. While it was agreed that specialisation could go too far (there are many branches a nurse can specialise in), there is considerable need for courses in teaching, in administration, and in public health until this subject is more generally taught in the basic course.

The Conference warned against overcrowding the curriculum. Special subjects, such as sociology or psychology, should be taught selectively in order to introduce the nurse to those parts of the subject which have an immediate bearing on her work.

In nurse training, considerable advance can be achieved by replacing antiquated and largely haphazard methods by techniques derived from modern education. Many countries have already gone far in this direction, for it is clear that every effort is needed to make the best use of available nursing personnel.

Another sphere in which modern knowledge can contribute to the improvement of nursing is the selection of candidates. Several speakers pointed out that there is no "ideal type of nurse" that can objectively be determined, but there clearly are well-defined characteristics which are undesirable in a profession that deals with human beings and whose laboratory is the community. These characteristics can be detected in the individual by psychological methods. In this way unsuitable candidates can be eliminated.

Insect Resistance to Insecticides

Leadership in the stimulation and co-ordination of research throughout the world on the problem of insect resistance to insecticides should be assumed by the World Health Organization according to a recommendation made by a group of experts at the conclusion of a week of meetings in Geneva.

Some of the most serious and widespread of the world's health problems are insect-borne diseases such as malaria, yellow fever, typhus, plague, filariasis (elephantiasis), kala azar, dysenteries, etc. The principal insects concerned are mosquitoes, flies of different kinds, fleas and lice. The use of modern insecticides like DDT has resulted in spectacular progress in controlling a number of these diseases and has produced substantial economic and social benefits in many of the countries concerned. Considerable alarm has, however, been caused by the appearance of resistance to these insecticides among certain species of the insects concerned. In 1955, the World Health Organization consequently urged its member countries to undertake campaigns aiming to eradicate malaria before the mosquitoes have time to develop resistance. The resistance problem was, therefore, the principal subject for discussion at the Seventh Session of WHO's Expert Committee of Insecticides.

According to the Committee's recommendations, WHO should aim to co-ordinate the different lines of research on the resistance problem already being undertaken in laboratories scattered throughout the world; stimulate further research, particularly in the physiology, biochemistry and genetics of the insects concerned; assure the publication and exchange of information and research

results; and facilitate the procurement of qualified personnel and funds for research.

The Nutrition Society

The 105th Meeting will be held at Guy's Hospital Medical School, London, S.E. 1, on Saturday, October 6th, 1956, and will take the form of a joint symposium with the Laboratory Animals Bureau on the Nutrition of Laboratory Animals.

Suicide as a Cause of Death since the Beginning of the XXth Century

In its first statistical survey of suicide as a cause of death since the beginning of this century, the World Health Organization (WHO) has been able to obtain data from 25 countries. Factors such as reluctance to certify a death as suicide because of the stigma attached to this act in many countries, and also failure to recognise a disguised suicide, have to be kept in mind in interpreting the figures.

In the 25 countries studied, with an adult population of 400 million people, from 71,000 to 72,000 men and women die by their own hand each year. This represents an average death rate of 17 to 18 per 100,000 adults.

The highest death rates from suicide in both sexes are found in Japan, Denmark, Austria and Switzerland. The lowest rates are reported in Ireland, Northern Ireland, Chile, Scotland and Spain. Within the U.S.A., the rate for the white population is almost three times that of the non-white population.

The WHO report shows that everywhere, men are much more prone to suicide than women. The ratio is in general roughly 3 to 1, but it varies from more than four to one in Norway to less than two to one in Japan. Highest rates for male suicides are recorded in Switzerland, Denmark, Austria and Finland. For women, they are to be found in Japan, Denmark and Austria.

CORRESPONDENCE

The Editor is not responsible for the views expressed by correspondents

Acute Tonsillitis and Pharyngitis

SIR,—Acute tonsillitis and pharyngitis are ailments from which most of the people suffer almost all the year round leading to much avoidable suffering and inconvenience. These are amenable to ordinary remedies.

A simple combination of the following drugs has been found to be very effective for irritations in the throat.

Throat paint:

R/	Pot. Chlor.	...	gr. 30
	Resorcin	...	gr. 40
	Acid Carbolic	...	m. 10
	Tinct. Lavendulae Co.	...	m. 20
	Spt. Menth Pip.	...	m. 30
	Glycerine pure ad.	...	oz. 1
	Ft. Pigment		

Similarly a combination of the following drugs has been found to be quite effective in irritation of the mouth and pharynx.

Gargle:

R/	Acid Carbolic	...	m. 200
	Pot. Bromide	...	dr. 4
	Sodi Bicarb.	...	dr. 4
	Spt. Menth Pip.	...	oz. 2
	Tinct. Lavendulae Co.	...	dr. 2
	Glycerine	...	oz. 16
	Ft. Gargle		

One teaspoonful in half a teacupful of warm water is used as gargle every 4 hours.

I have tried these in innumerable cases and have found them to be extremely useful. I do not claim any originality. The combinations have been arrived at after various trials.

I would request my colleagues to try these simple drugs before resorting to either antibiotics or more expensive methods of treatment. I am etc.

Lucknow. R. N. KACKER, M.B.B.S., D.L.O. (R.C.S., ENG.), Z.L.O. (VIENNA).

A Study of a Few Cases of Yaws in Cooch Behar

SIR,—Yaws is a contagious disease occurring in tropical humid areas, near the foot of hills, characterised by macular, lichenous rash, papillomatous fambroesioma at its different stages.

I have come across a few cases of yaws in Cooch Behar district, in West Bengal. Seven typical cases are described.

CASE 1—An 11 year old female had punched out ulcer on both heels with a diameter 2 cm. for 2 years. The floor of the ulcers were covered with black slough. The patient complained of pain in walking.

Case 2—A 30 year old female had a punched out ulcer (1 cm. diam.) on the right heel and a raspberry-like granulomatous growth (2 cm. diam.) on the plantar aspect of the left great toe for 1 year 3 months. She had difficulty in walking.

Case 3—A 25 year old male had a raw fungating papillomatous growth (3 cm. diam.) on the right heel, and a punched out ulcer (2 cm. diam.) on the anterior part of the sole of the left foot for 3 years. He complained of difficulty in walking.

Case 4—A 30 year old male had a raspberry-like growth on the left thenar eminence (3 cm. diam.) for 1½ years.

Case 5—A 35 year old male had a punched out ulcer on the right heel (2·5 cm. diam.) and one warty growth (2 cm. diam.) on the plantar aspect of the right first metatarsophalangeal joint. A raspberry-like growth (3 cm. diam.) on the anterior part of the sole of the left foot for 1½ years.

Case 6—A 45 year old male had a granulomatous warty growth (3·5 cm. diam.) on the middle of the sole of the right foot. One small indurated ulcer (1·5 cm. diam.) on the plantar aspect of the left great toe for 3 years.

Case 7—A 26 year old male had a raspberry-like growth (3 cm. diam.) on the outer side of the sole of the left foot and a small warty growth (1·8 cm. diam.) on the plantar aspect of the right first metatarsophalangeal joint for 4½ years.

All the cases were treated with ten I.M. injections of diethylamine acetarsol (3 c.c.) twice a week. The growths were treated with a paint consisting of acid salicylic 40 grains, and benzoic 30 grains, in an ounce of collodion flexile. The secondary infections in three cases were treated with penicillin—12 lakhs units intramuscularly once a week for 4 injections. All the cases were cured clinically. Periodical check up was done fortnightly after cure upto 3 months, except in Case 6 who did not turn up after cure. No relapse was noted.

Cooch Behar is a humid place with extremes of climate. The people affected are the original cultivator class of the district. The cases were chronic in nature and had no seasonal prevalence. Sites affected were mainly, sole of the feet, except in one case where the palm was affected. In no case was there any glandular enlargement, history of exposure to V.D., eye lesion or scar on the genitalia. Kahn test in all the cases except one was negative.

From my experience in the past about the appearance and treatment of yaws cases in Malaya, Chin Hills, Lushai Hills and Garo Hills area amongst the aboriginal people of those lands, the cases under review in my opinion were of yaws.

My cordial thanks to Dr. R. R. Roy, Surgeon Superintendent, M. J. N. Hospital, Cooch Behar, West Bengal, for his guidance and kind permission to communicate this report for publication. Thanks are also due to Dr. B. N. Bhattacharjee, Emergency Officer, M. J. N. Hospital, Cooch Behar for his kind help. I am etc.

M. J. N. Hospital,
Cooch Behar. B. C. CHAKRABORTI, L.M.F.
M.O., O.P.D.

REVIEWS

Hand Book of Legal Medicine—By Louis J. Regan and Alan R. Moritz; 21·6×14 cm., pp. 201, 1956. The C. V. Mosby Co., St. Louis.

Medical practice in modern times deserves a high ethical standard and a conscious insistence on the relationship between the members of the profession and the general public. This very handy compilation should be welcomed by those doctors who are especially interested in the branch of legal medicine. The authors' language is lucid and evidently they have written it from the practical point of view. They have touched almost all the points with special elaborations of those items where the physician-patient relationship might have the chance to come to conflict. Illustrations are many and add to the usefulness of the volume.

Peripheral Vascular Disorder—Edited by Peter Martin, R. Beverley Lynn, J. Henry Dible and Ian Aird. 847 pages with 568 illustrations, 35 in colour. First Edition 1956. E. & S. Livingstone Ltd., Edinburgh and London. Price £5 10s.

The volume can be said to be a masterpiece on vascular surgery. The reputed authors must have worked for years to have incorporated so many references in one book. Prof. Aird has already made a name for himself for such enormous reference work in his other book.

The method of approach in each subject is unique. The chapter on Plethysmograph is unparalleled. The physiology of circulation is well explained. The book has covered all the known disorders. The short chapter of Anatomy of the Vessels has not been at par with the other chapters. There are a few sweeping remarks in the chapters on Parasitic Lymphaedema and Venography in varicose veins, which are better avoided in a book of this standard as quite a lot of these problems are still far from solved. There is no mention about intraosseous venography. Typography and photographic reproductions are quite good.

International Record of Medicine and General Practice Clinics—Symposium on Medical Writing (Vol. 168, No. 10, October, 1955)—Published by M. D. Publications, Inc., 30 East 10th Street, New York 22, N.Y., U.S.A. Subscription rate—foreign $12.00 per year, single copy $1.40.

The symposium contains over 60 pages of very readable and interesting articles from the pen of well-known authors, carefully chosen to write on this important subject; this is of importance to-day in view of the colossal number of medical articles published throughout the world. These articles should be seriously studied by all who are concerned with medical writing, including editing of the same, and especially by young and prospective authors of scientific medical articles.

IV RAJPUTANA PROVINCIAL MEDICAL CONFERENCE, AJMER

The Fourth Rajputana Provincial Medical Conference will be held at Ajmer on 29-30 September and 1 October, 1956. Symposia on Coronary Heart Disease and Renal Lithiasis have been arranged. Details may be had from Dr. B. M. Sharma, Organising Secretary of the Conference, Ajmer.

* * * * * *

VIII M. P. PROVINCIAL MEDICAL CONFERENCE, NAGPUR

The Eighth M. P. Provincial Medical Conference will be held at Nagpur on 7-9 October 1956 (The dates are provisional). A Scientific Session and a Scientific Exhibition will be held, also a Souvenir published. Members of the profession are requested to extend their full co-operation to this conference. Detailed information may be had from the Organising Secretary of the Conference, Dhanwate Chambers Annexe, Sitalbaldi, Nagpur-1.

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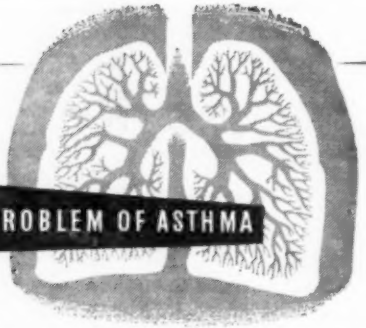

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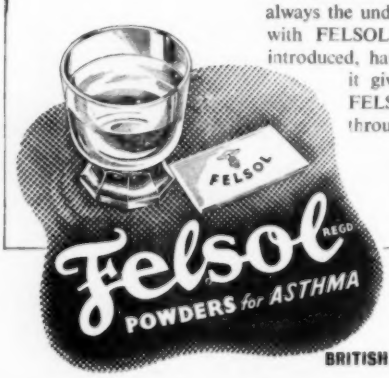

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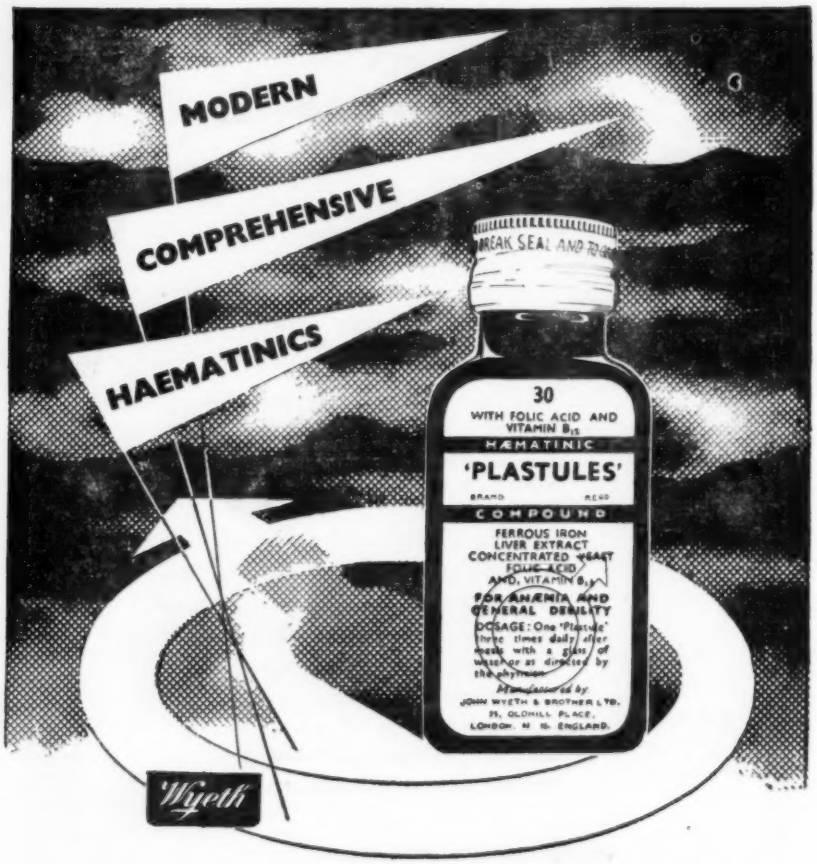

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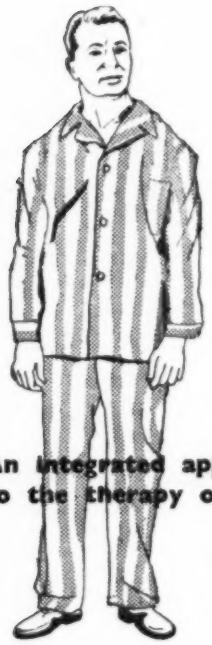

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